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NEURODEVELOPMENT, QUALITY OF LIFE AND BURDEN OF CARE OF YOUNG CHILDREN WHO HAVE UNDERGONE CARDIAC INTERVENTIONS IN CENTRAL SOUTH AFRICA: THREE-MONTH AND SIX-MONTH POST CARDIAC INTERVENTION OUTCOMES

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A thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

Over recent decades medical and surgical advances have significantly lowered the mortality rate for children born with congenital heart defects. Congenital heart disease (CHD) survivors are at high-risk of growth retardation and developmental morbidity that negatively affect their health-related quality of life (HRQOL). In addition, caring for a child with a chronic health condition such as CHD places a considerable financial and emotional burden on parents, putting them at risk of ongoing stress and psychological morbidity including anxiety and depression. The outcomes of children living with CHD and their families in South Africa (SA) are unknown. Outcomes for children with CHD in SA are likely to be further complicated by social disadvantage and Human Immunodeficiency Virus (HIV) co-infection.

The aim of this observational descriptive study (Phase I and II) was to determine the pre-cardiac intervention, and three-month and six-month post-cardiac intervention development, growth, HRQOL and parenting stress outcomes of young children with CHD in central SA. Outcomes were compared over time, and variables associated with development, HRQOL and parenting stress outcomes determined. In addition, the developmental needs of young children living with CHD in central SA were to be identified.

In order to meet the Phase I and II objectives, forty-eight consecutive children, 30 months and younger, and their parents were recruited into this study at the Universitas Academic Hospital in Bloemfontein. Children who had previous or emergency cardiac surgery were excluded. Development was assessed using the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III), HRQOL using the Paediatric Quality of Life Inventory (PedsQL^{TM}) and levels of parenting stress using the Parenting Stress Index Short-Form (PSI-SF). Growth outcomes were determined by z-scores calculated for growth parameters. Medical severity of the cardiac disease was rated by a paediatric cardiologist using the Cardiologists Perception of Medical Severity Scale.

Baseline data was collected for 40 children. The majority of children (n=26) underwent open-heart surgery in infancy with cardiopulmonary bypass. Most children (n=30) had moderate disease severity, with twenty percent (n=8) having cyanotic heart defects. A quarter of the children (n=10) had Down syndrome (DS). Surgical outcomes were

comparable to those reported in developed countries, with a mortality rate of 15%. There was a high attrition rate during Phase II of this study, with 47.5% of children and their families missing one or more follow-up visit. Mothers fulfilled the role of primary caregiver, and carried most of the burden of care. The majority of families were from a low socioeconomic backgrounds (87.5%) and mothers had low levels of education, with only 40% having graduated high school.

The majority (68%) of children had suboptimal growth prior to cardiac intervention. There was significant growth catch-up for both weight ($p=0.04$) and head circumference ($p= 0.02$) by the six-month post-cardiac intervention. Complete catch-up growth had not yet taken place by the six-month post-cardiac intervention, with 40.9% of the children still presenting with malnutrition. The growth trends of children with CHD with DS were found to be similar to those of children with CHD without DS. Growth in children with cyanotic heart defects tended to be poorer both before and after cardiac intervention.

There was a high prevalence of moderate developmental delay across all development domains. Motor delays (27.5%) were most prevalent prior to cardiac intervention. Motor performance improved with age and post cardiac intervention, but language and cognitive performance declined with age and increasing skill complexity. There was not a significant change in the developmental outcome of the children over the time-span of this study. The developmental outcome for children with cyanotic heart defects tended to be similar to those with acyanotic heart defects. The presence of DS was significantly ($p<0.001$) associated with developmental outcome across all developmental domains at all time-points of assessment. Children with CHD with DS tended to have considerably poorer developmental outcomes compared to children with CHD without DS. Disease severity ($p=0.02$) and maternal age ($p=0.01$) were significantly associated with cognitive development. Age at first cardiac surgery was found to be significantly associated with language development both before cardiac intervention ($p<0.01$) and at three-month post-cardiac intervention ($p=0.04$). Suboptimal growth prior to cardiac intervention ($p=0.04$) and maternal age ($p<0.001$) were significantly associated with motor development. Developmental performance was well below the test mean on all subscales of the BSID-III at all the time points of assessment. Although the patterns of development and the prevalence of developmental delays in the current study were similar to those reported in developed

countries, children living with CHD in central SA performed below the expected developmental levels for children with CHD when assessed on the BSID-III. Hypotonia was the most significant abnormal neurological finding, with 45% of the children presenting with hypotonia prior to cardiac intervention. The hypotonia tended to resolve in the children without DS by the six-month post-cardiac intervention.

Overall parents' perceived their children's HRQOL as being relatively good, and similar to that of their healthy same-aged peers and other children with CHD in developed countries. Parents' perception of their children's HRQOL improved significantly after cardiac intervention ($p= 0.04$). Perceived HRQOL tended to be similar for children with cyanotic and acyanotic heart defects. Parents of children with CHD with DS tended to perceive their children's HRQOL as poorer when compared with parents of children with CHD without DS. Motor development ($p=0.01$) and levels of parenting stress ($p=0.02$) were significantly associated with parents' perceptions of their children's HRQOL prior to cardiac intervention.

The majority of parents' (60%) experienced clinically significant levels of stress prior to their children undergoing cardiac intervention. Parenting stress decreased significantly from pre-cardiac intervention levels at both three-month ($p<0.001$) and six-month ($p<0.001$) post-cardiac intervention as the child's cardiac symptoms resolved or decreased, and their health status improved. Parents of children with cyanotic and acyanotic heart defects tended to experience similar levels of stress. Parents of children with CHD with DS tended to experience higher levels of ongoing stress when compared with parents of children with CHD without DS. Parenting stress prior to cardiac intervention was significantly associated with parents' perception of their child's HRQOL ($p=0.02$) and language development ($p=0.04$). Parenting stress at three-month post-cardiac intervention was significantly associated with age at first cardiac surgery ($p=0.03$), language development ($p=0.03$) and level of maternal education ($p=0.04$). HRQOL and parenting stress outcomes were closely linked before cardiac intervention. Parents perceiving their child as having a poor ability to function in everyday situations experienced increased stress levels.

Based on developmental performance on the BSID-III 59% of the children in the current study would qualify for referral to early intervention (EI) services including physiotherapy, occupational therapy and speech therapy, with many children requiring

access to more than one service. A home-based parent-driven developmental activity programme would likely be best suited to meet the developmental needs of children with CHD living in central SA taking into account the geography of the area and service delivery challenges in the public healthcare sector.

Phase III of the study resulted in the development of a home-based developmental activity programme to meet the identified developmental needs of children with CHD in central SA. Qualitative methods, including an expert panel of rehabilitation professionals and a focus group of parents, were used to gain consensus on the content of the developmental activity programme.

In conclusion, it is encouraging that the longer-term outcomes of children with CHD in central SA were not vastly different from those of children in developed countries. The greater extent of the growth retardation and developmental delay of the children in the current study is however of concern. The findings in this study strongly support the implementation of a cardiac neurodevelopmental programme as part standard cardiac care in SA. Early developmental intervention and psychosocial support services are indicated to optimise the outcome for both children living with CHD and their families. A home-based parent-driven developmental stimulation programme provides an innovative approach to meeting the developmental needs of young children living with CHD.

Keywords

Congenital heart disease, neurodevelopment, growth, parenting stress, health-related quality of life, home-based developmental activity programme, Bayley Scales of Infant and Toddler Development, Third Edition, Paediatric Quality of Life Inventory, Parenting Stress Index-Short Form.

DECLARATION

I Robyn Smith declare that this thesis is my own, unaided work. It has been submitted for the Degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

_____

20th day of September 2017 in Johannesburg

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Nelson Mandela

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The abstract entitled “Influence of cardiac intervention on neurodevelopment in young children with congenital heart disease in central South Africa: Three-month and six-month outcomes" has been accepted for presentation at the 7th World Congress of Paediatric Cardiology and Cardiac Surgery (WCPCCS) which will take place in Barcelona, Spain from 16 to 21 July 2017.

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TABLE OF CONTENTS

ABSTRACT i

DECLARATION v

ACKNOWLEDGEMENTS vi

FUNDING ACKNOWLEDGEMENTS viii

PUBLICATIONS AND PRESENTATIONS IN SUPPORT OF THIS THESIS..... ix

TABLE OF CONTENTS x

LIST OF TABLES xxii

LIST OF FIGURES xxiv

LIST OF ABBREVIATIONS xxvi

DEFINITION OF TERMS xxx

CHAPTER 1: INTRODUCTION 1

1.1 Congenital heart disease: A global perspective 1
1.2 Congenital heart disease: An African perspective 4
1.3 Problem statement 8
1.4 Research questions 9
1.5 Aims 10
1.6 Objectives 10
1.6.1 Main objectives 10
1.6.2 Secondary objectives 11
1.7 Significance of the study 12
1.8 Organisation of the thesis 13

CHAPTER 2: LITERATURE REVIEW 14

2.1 INTRODUCTION 14

2.2 CONGENITAL HEART DISEASE IN CHILDREN 16

2.2.1 Risk factors for congenital heart disease 16
2.2.2 Prevalence and survival 16
2.2.3 Classification of congenital heart defects 17
2.2.3.1 Classification based on the nature of the defect 17
2.2.3.2 Classification based on the medical severity 17
2.2.4 Management of congenital heart disease 18
2.2.5 Summary 18

2.3 NEURODEVELOPMENTAL OUTCOME IN CHILDREN WITH CONGENITAL HEART DISEASE 19

2.3.1 Introduction 19
2.3.2 Brain abnormalities associated with congenital heart disease 20
2.3.2.1 Genetic susceptibility 21
2.3.2.2 Structural differences in the brain 21
2.3.2.3 Acquired brain injury 22
2.3.3 Abnormal neurological examinations 23
2.3.4 Risk factors for poor neurodevelopmental outcome 24
2.3.4.1 Type and severity of the congenital heart disease 25
2.3.4.2 Surgery in early infancy 25
2.3.4.3 Cyanotic heart defects not requiring surgery in infancy 26
2.3.4.4 Peri-operative risk factors 26
2.3.4.4.1 Cardiopulmonary bypass 27
2.3.4.4.2 Deep hypothermic circulatory arrest 27
2.3.4.4.3 Aorta cross-clamp time 28
2.3.4.5 Medical complications and haemodynamic instability in the post-operative period ... 29
2.3.4.5.1 Cardiopulmonary resuscitation 29
2.3.4.5.2 Prolonged hospital length of stay 30
2.3.4.5.3 Peri-operative seizures and stroke 30
2.3.4.6 Patient-specific risk factors 31
2.3.4.6.1 Prematurity and low birth weight 31

2.3.4.6.2 Genetic abnormalities associated with developmental disorders 31
2.3.4.6.3 Neuroimaging abnormalities and microcephaly 32
2.3.4.6.4 Gender and ethnicity 32
2.3.4.6.5 Feeding problems and growth failure 33
2.3.4.6.6 Sociodemographic factors 33
2.3.5 Neurodevelopmental outcome in children with congenital heart disease 34
2.3.5.1 Introduction 34
2.3.5.2 Patterns of developmental delay and impairment 35
2.3.5.2.1 Motor development 36
2.3.5.2.2 Cognitive development 38
2.3.5.2.3 Language development 39
2.3.5.2.4 Behavioural and psychosocial outcomes 40
2.3.6 Developmental outcomes in children with congenital heart disease and Down syndrome 41
2.3.7 Decreasing developmental morbidity in children with congenital heart disease: Implications for clinical practice 43
2.3.8 Childhood development in developing countries 44
2.3.9 Summary 45

2.4 GROWTH FAILURE AND FEEDING DIFFICULTIES IN CHILDREN WITH CONGENITAL HEART DISEASE 47

2.4.1 Introduction 47
2.4.2 Growth trends in children with congenital heart disease 47
2.4.3 Malnutrition and growth failure in children with congenital heart disease 47
2.4.4 Causes of growth failure in children with congenital heart disease 49
2.4.4.1 Inadequate calorie intake 49
2.4.4.2 Increased metabolism 49
2.4.4.3 Inadequate and ineffective nutrient absorption 50
2.4.4.4 Additional factors contributing to growth failure 50
2.4.5 Growth outcomes in children with congenital heart disease 51
2.4.6 Growth outcomes in children with congenital heart disease and Down syndrome 54
2.4.7 Feeding problems in children with congenital heart disease 55
2.4.8 Relationship between growth and developmental outcome in children with congenital heart disease 56
2.4.9 Growth in children in developing countries 57
2.4.10 Reducing growth failure in children with congenital heart disease: Implications for clinical practice 58

2.4.11 Summary 58

2.5 HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH CONGENITAL HEART DISEASE 59

2.5.1 Introduction 59
2.5.2 Defining quality of life, health-related quality of life and wellbeing 60
2.5.3 Factors affecting health-related quality of life in children with congenital heart disease 61
2.5.4 Establishing health-related quality of life in children with congenital heart disease 63
2.5.5 Health-related quality of life outcomes in children with congenital heart disease 65
2.5.6 Health-related quality of life outcomes in children with congenital heart disease and Down syndrome 69
2.5.7 Improving health-related quality of life outcomes in children with congenital heart disease: Implications for clinical practice 70
2.5.8 Summary 71

2.6 PARENTING STRESS AND THE BURDEN OF CARING FOR A CHILD WITH CONGENITAL HEART DISEASE 72

2.6.1 Introduction 72
2.6.2 Stressors associated with psychosocial morbidity in parents of children with congenital heart disease 73
2.6.2.1 Diagnosis, hospitalisation and cardiac surgery 74
2.6.2.2 Role stress and burden of care 75
2.6.2.3 Feeding difficulties and growth failure 75
2.6.2.4 Severity of the congenital heart disease 76
2.6.2.5 Age and characteristics of the child 76
2.6.2.6 Socioeconomic conditions and cost of care 78
2.6.2.7 Low levels of parent education 79
2.6.2.8 Family strain 79
2.6.2.9 Marital strain 79
2.6.2.10 Lack of social support 80
2.6.3 Psychological morbidity in parents of children with congenital heart disease 80
2.6.4 Parenting stress outcomes in children with congenital heart disease 81
2.6.5 Parenting stress outcomes in children with congenital heart disease and Down syndrome 82
2.6.6 Parenting stress outcomes in resource-poor communities 83

2.6.7 Parenting a child in a developing country 84
2.6.8 Reducing psychosocial morbidity in parents of children with congenital heart disease: Implications for clinical practice 84
2.6.9 Summary 85

2.7 THE BURDEN OF CARING FOR A CHILD WITH CONGENITAL HEART DISEASE 86

2.7.1 Introduction 86
2.7.2 The financial burden of caring for a child with congenital heart disease 86
2.7.3 Educational attainment and the occupational prestige of parents 88
2.7.4 Summary 89

CHAPTER 3: OUTCOME MEASURES AND PILOT STUDY 90

3.1 Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) 90

3.1.1 Description of the BSID-III scales 90
3.1.2 Administration and scoring procedures for the BSID-III 91
3.1.3 Standardisation and norming of the BSID-III 93
3.1.4 Reliability and validity of the BSID-III 93
3.1.5 Concerns regarding the BSID-III 94
3.1.6 Use of the BSID-III as a measure of development in the South African population 95
3.1.7 Use of the BSID-III as a measure of development in children with congenital heart disease 95
3.1.8 Permission to use the BSID-III 96

3.2 Parenting Stress Index Short Form (PSI-SF) 96

3.2.1 Description of the PSI-SF subscales 96
3.2.2 Administration and scoring of the PSI-SF 97
3.2.3 Standardisation and norming of the PSI-SF 97
3.2.4 Reliability and validity of the PSI-SF 97
3.2.5 Use of the PSI-SF as a measure of parenting stress in the South African population 98

3.2.6 Use of the PSI-SF as a measure of parenting stress in children with congenital heart disease 98
3.2.7 Permission to use the PSI-SF 99
3.2.8 Translation of the PSI-SF 99

3.3 Paediatric Quality of Life Inventory (PedsQL™) 99

3.3.1 Development of the PedsQL™ 99
3.3.2 Description of the PedsQL™ scales and modules used 99
3.3.2.1 PedsQL™ Infant Scales 100
3.3.2.2 PedsQL™ 3.0 Cardiac Module 100
3.3.3 Administration and scoring of the PedsQL™ 100
3.3.3.1 Scoring of the PedsQL™ Infant Scales 100
3.3.3.2 Scoring of the PedsQL™ 3.0. Cardiac Module 101
3.3.4 Standardisation and norming of the PedsQL™ Infant Scales and Cardiac Module 101
3.3.5 Reliability and validity of the PedsQL™ 101
3.3.6 The use of the PedsQL™ as a measure of health-related quality of life in the South African population 102
3.3.7 Use of the PedsQL™ as a measure of health-related quality of life in children with congenital heart disease 102
3.3.8 Permission to use the PedsQL™ 102
3.3.9 Translation of the PedsQL™ 103

3.4 Hollingshead Socioeconomic Index and Hollingshead Index of Social Position 103

3.4.1 Determinants of Hollingshead's Four Factor Index of Social Status 103
3.4.2 Calculation and interpretation of the Hollingshead indices 103
3.4.2.1 Hollingshead Socioeconomic Index 103
3.4.2.2 Hollingshead Index of Social Position 104
3.4.3 Reliability and validity of the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position 104
3.4.4 Use of the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position as a measure of social status in the South African population 105
3.4.5 Use of the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position as a measure of social status in families of children with congenital heart disease 105

3.4.6 Concerns regarding the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position 105
3.4.7 Permission for use of the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position 106

3.5 Pilot study 106

3.6 Conclusion 109

CHAPTER 4: METHOD FOR PHASE I AND PHASE II 110

4.1 Study location 110
4.2 Ethical considerations 111
4.3 Study design 112
4.4 Participants 113
4.5 Materials and measurements 114
4.5.1 Demographic information of the child and family 114
4.5.2 Socioeconomic status of the family 114
4.5.3 Cardiac diagnosis and medical management information 115
4.5.4 Cardiovascular status 115
4.5.5 Surgical intervention and post-operative medical course information 116
4.5.6 Anthropometric measurements 116
4.5.7 Neurodevelopmental status 117
4.5.8 Neurological status 118
4.5.9 Neurodevelopmental risk stratification 118
4.5.10 Health-related quality of life 119
4.5.11 Parenting stress 119
4.5.12 Burden of care 119
4.6 Procedure for Phase I and Phase II 120
4.7 Measures to limit attrition 126
4.8 Statistical analysis 127

CHAPTER 5: RESULTS OF PHASE I AND PHASE II 129

5.1 Study attrition 130
5.2. Baseline sociodemographic information for all participants 137
5.2.1 Demographic information 137
5.2.2 Socioeconomic status 139
5.3 Cardiac diagnostic and medical management information 142
5.4 Surgical intervention and post-operative medical course 148
5.5 Growth outcomes 152
5.6 Neurodevelopmental outcomes 156
5.7 Neurological findings 164
5.8 Parents' perception of health-related quality of life 165
5.9 Parenting stress outcomes 170
5.10 Burden of care 175
5.11 Changes in key outcomes over time 177
5.12 Variables associated with key outcomes 179
5.12.1 Variables associated with neurodevelopmental outcome 180
5.12.2 Variables associated with parents' perception of health-related quality of life 187
5.12.3 Variables associated with levels of parenting stress 189
5.13 Key outcomes for groups of special interest 191
5.13.1 Outcomes for children with CHD with Down syndrome compared to those with CHD without Down syndrome 192
5.13.1.1 Sociodemographic information 192
5.13.1.2 Cardiology diagnostic information 192
5.13.1.3 Surgical intervention and post-operative medical course 193
5.13.1.4 Growth outcomes 193
5.13.1.5 Neurodevelopmental outcomes 195
5.13.1.6 Parents' perception of health-related quality of life 198
5.13.1.7 Parenting stress outcomes 199
5.13.2 Outcomes for children with cyanotic versus acyanotic heart defects 202
5.13.2.1 Sociodemographic information 202
5.13.2.2 Cardiology diagnostic information 202
5.13.2.3 Surgical intervention and post-operative medical course 203
5.13.2.4 Growth outcomes 203
5.13.2.5 Neurodevelopmental outcomes 205
5.13.2.6 Parents' perception of health-related quality of life 207
5.13.2.7 Parenting stress outcomes 208

5.14 Summary 209

CHAPTER 6: DISCUSSION 211

6.1 Recruitment, sample size and study attrition. 211
6.2 Sociodemographic information 216
6.3 Congenital heart disease profile 219
6.4 Surgical intervention and post-operative medical course 220
6.5 Growth outcomes 223
6.5.1 Growth outcomes as reflected by z-scores 223
6.5.2 Change in growth outcomes over time 225
6.5.3 Relationship between growth and neurodevelopmental outcomes 226
6.6 Neurodevelopmental outcomes 227
6.6.1 Developmental performance on the BSID-III 227
6.6.2 Prevalence of developmental delays 230
6.6.3 Developmental profile 232
6.6.4 Gross motor developmental performance in prone 233
6.6.5 Significant neurological sequelae 235
6.6.6 Qualification for access to early intervention services based on developmental performance 235
6.6.7 Change in developmental outcomes over time 237
6.6.8 Variables associated with neurodevelopmental outcomes 237
6.7 Neurological findings 241
6.8 Parents' perception of health-related quality of life 242
6.8.1 Parents' perception of health-related quality of life outcomes as reflected by PedsQL™ scores 242
6.8.1.1 Health-related quality of life outcomes for children younger than two years 242
6.8.1.2 Health-related quality of life outcomes for children older than two years 243
6.8.1.3 Health-related quality of life outcomes for all children 245
6.8.2 Changes in parents' perception of health-related quality of life over time 245
6.8.3 Variables associated with health-related quality of life outcomes 246
6.9 Parenting stress and burden of care 249
6.9.1 Parenting stress outcomes 249
6.9.2 Changes in parenting stress over time 250
6.9.3 Burden of care and parent stressors 250
6.9.3.1 Illness-related stressors 251
6.9.3.2 Parent-related stressors 251

6.9.3.3 Child-related stressors 252
6.9.3.4 Socioeconomic-related stressors 252
6.9.4 Variables associated with levels of parenting stress 252
6.10 Outcomes in children with congenital heart Down syndrome 254
6.10.1 Introduction 254
6.10.2 Growth outcomes 255
6.10.3 Developmental outcomes 256
6.10.4 Parents' perception of health-related quality of life outcomes 257
6.10.5 Parenting stress outcomes 257
6.11 Outcomes in children with cyanotic heart defects 258
6.11.1 Growth outcomes 258
6.11.2 Developmental outcomes 259
6.11.3 Parents' perception of health-related quality of life outcomes 259
6.11.4 Parenting stress outcomes 260
6.12 Strengths of this study 260
6.13 Challenges encountered during the study 261
6.13.1 Logistical challenges 261
6.13.2 Loss to follow-up 262
6.13.3 Assessment measures 263
6.14 Study limitations 264
6.15 Clinical recommendations 265
6.16 Research implications 267
6.17 Conclusion 270

CHAPTER 7: DEVELOPMENT OF A HOME-BASED DEVELOPMENTAL ACTIVITY PROGRAMME (PHASE III) 274

7.1 Introduction 275
7.2 Literature review 275
7.2.1 Theoretical frameworks 275
7.2.1.1 Family-centred care 276
7.2.1.2 International Classification of Functioning, Disability and Health (ICF) 276
7.2.2 Early developmental intervention 278
7.2.2.1 Components of early intervention programmes 279
7.2.2.2 Effectiveness of early intervention programmes 280
7.2.3 Home programmes 280
7.2.3.1 Components of home programmes 281

7.2.3.2 Effectiveness of home programmes 283
7.2.4 Developmental intervention in children with congenital heart disease 284
7.2.4.1 Evidence-based approach to developmental intervention in children with congenital heart disease 284
7.2.4.2 Early developmental intervention for children with congenital heart disease 285
7.2.4.3 The use of prone positioning as a developmental position in children with congenital heart disease 288
7.2.4.4 Physical activity prescription in young children with congenital heart disease 288
7.3 Rationale and development of the home-based parent-driven developmental activity programme 292
7.3.1 Introduction 292
7.3.2 Rationale behind the home-based parent-driven developmental activity programme 293
7.3.3 Development of the home-based parent-driven developmental activity programme 294
7.4 Method for Phase III 297
7.4.1 Location 297
7.4.2 Ethical considerations 297
7.4.3 Study design 298
7.4.4 Participants 298
7.4.4.1 Focus group 298
7.4.4.2 Expert panel 299
7.5 Procedure for Phase III 300
7.5.1 Focus group 301
7.5.2 Expert panel 302
7.6 Interpretation of the findings from the focus group and expert panel 303
7.6.1 Focus group 303
7.6.2 Expert panel 305
7.7 Presentation of the parent information document 307
7.8 Presentation of the home-based parent-driven developmental activity programme 307
7.9 Suggested model for implementation of the home-based parent-driven developmental activity programme 307

CHAPTER 8: CONCLUSION 308

REFERENCES **313**

APPENDICES **369**

APPENDIX I: Classification of congenital heart disease based on the nature of the defect
APPENDIX II: Classification of congenital heart disease based on medical severity
APPENDIX III: User agreement for the BSID-III
APPENDIX IV: User agreement for the PSI-SF
APPENDIX V: User agreement for the PedsQL™
APPENDIX VI: Ethical clearance certificates
APPENDIX VII: Permission letters from relevant authorities
APPENDIX VIII: Parent information letter and informed consent form: Phase I and II.
APPENDIX IX: Data form: Demographic information of the child and family
APPENDIX X: Data form: Cardiac diagnosis, and medical and surgical management
APPENDIX XI: Data form: Cardiovascular, growth and neuromotor status
APPENDIX XII: Data form: Burden of care at three-month and six-month post cardiac intervention
APPENDIX XIII: Data form: Path through the study
APPENDIX XIV: Regression analysis: Variables predictive of key outcomes
APPENDIX XV: Outcomes of children with congenital heart disease with Down syndrome
APPENDIX XVI: Outcomes of children with cyanotic heart defects
APPENDIX XVII: HRQOL outcomes on the PEDSQL™ Infant Scales
APPENDIX XVIII: Parent information letter and informed consent form: Phase III
APPENDIX IXX: Expert panel information and informed consent letter: Phase III
APPENDIX XX: Parent information document on congenital heart disease
APPENDIX XXI: Developmental activity programme
APPENDIX XXII: Proposed model for the implementation of the developmental activity programme
APPENDIX XXIII: “Turnitin” similarity report

LIST OF TABLES

Chapter 2: Literature review

Table 2.1 CHD complexity and presence and severity of developmental disability 36

Chapter 3: Outcome measures and pilot study

Table 3.1 BSID-III composite scores and standard deviation equivalents 92
Table 3.2 Descriptive classifications of the BSID-III composite scores 93
Table 3.3 Social class according to the Hollingshead Socioeconomic Index scores .. 104
Table 3.4 Social class categories for the Hollingshead Index of Social Position scores 104

Chapter 5: Results of Phase I and Phase II

Table 5.1 Attrition analysis for key child-related variables at baseline 135
Table 5.2 Attrition analysis for key family-related variables at baseline 136
Table 5.3 Demographic information of the child 138
Table 5.4 Demographic information of the family 139
Table 5.5 Socioeconomic status of the families 141
Table 5.6 Distance travelled to the cardiac service point 143
Table 5.7 Cardiac diagnosis and congenital heart disease classification 145
Table 5.8 Medical information of importance 147
Table 5.9 Information pertaining to the cardiac surgery 149
Table 5.10 Medical course following surgery 151
Table 5.11 Anthropometric data 153
Table 5.12 Participants with malnutrition, stunting and microcephaly 154
Table 5.13 Age at neurodevelopmental assessment 156
Table 5.14 Cognitive, language and motor outcomes on the BSID-III 157
Table 5.15 Classification of developmental performance 159
Table 5.16 Children qualifying for early intervention services based on developmental performance 162
Table 5.17 Presence of abnormal muscle tone 164

Table 5.18 Perceived health-related quality of life of children one to 24 months 166
Table 5.19 Perceived health-related quality of life of children older than two years 168
Table 5.20 Perceived health-related quality of life for all children 169
Table 5.21 Parenting stress of the primary caregivers 171
Table 5.22 Classification of the levels of parenting stress 173
Table 5.23 Burden of care across the study 175
Table 5.24 Changes in key outcomes over time 178
Table 5.25 Variables associated with the BSID-III cognitive scores 181
Table 5.26 Variables associated with the BSID-III language scores 183
Table 5.27 Variables associated with the BSID-III motor scores 185
Table 5.28 Variables associated with the parents' perception of health-related quality of life 188
Table 5.29 Variables associated with levels of parenting stress 190
Table 5.30 Growth outcomes in children with CHD with DS compared to those with CHD without DS. 194
Table 5.31 Developmental outcomes on the BSID-III for children with CHD with DS compared to those with CHD without DS 196
Table 5.32 Perceived health-related quality of life outcomes of children with CHD with DS compared to those with CHD without DS 198
Table 5.33 Levels of parenting stress in children with CHD with DS compared to those with CHD without DS 200
Table 5.34 Growth outcomes for children with cyanotic heart defects compared to those with acyanotic heart defects 204
Table 5.35 Developmental outcomes on the BSID-III for children with cyanotic heart defects compared to those with acyanotic heart defects 206
Table 5.36 Perceived health-related quality of life outcomes for children with cyanotic heart defects compared to acyanotic heart defects 207
Table 5.37 Levels of parenting stress for children with cyanotic heart defects compared to acyanotic heart defects 208

LIST OF FIGURES

Chapter 1: Introduction

Figure 1.1 Total annual births of children with CHD per continent 4
Figure 1.2 African countries with cardiac programmes 6

Chapter 2: Literature review

Figure 2.1 Pathways from poverty to poor development 45
Figure 2.2 Potential influences on growth in children with CHD 51
Figure 2.3 Relationship between cardiac disease-related morbidity and HRQOL 61

Chapter 3: Outcome measures and pilot study

Figure 3.1 Theoretical model of the PSI-SF 96

Chapter 4: Method for Phase I and Phase II

Figure 4.1 Map of the provinces of South Africa 111
Figure 4.2 Flow diagram of the study procedure 125

Chapter 5: Results Phase I and Phase II

Figure 5.1 Loss to follow-up over the study 131
Figure 5.2 Classification of the type of congenital heart disease based on the presence of cyanosis 144
Figure 5.3 Mean z-scores for growth parameters over the study 155
Figure 5.4 Mean composite BSID-III subscale scores across the study 158
Figure 5.5 Average prevalence of developmental delays across the study 161
Figure 5.6 Children qualifying for early intervention services 163
Figure 5.7 Mean PedsQL™ total scores across the study 170
Figure 5.8 Mean total stress scores across the study 174
Figure 5.9 Prevalence of Down syndrome in this study sample 192
Figure 5.10 Prevalence of cyanotic heart defects in this study sample 202

Chapter 7: Development of the home-based developmental activity programme

Figure 7.1 The ICF-CY model 277
Figure 7.2 FITT principles of exercise prescription 290

LIST OF ABBREVIAITONS

AAP	American Academy of Paediatrics
ACSM	American College of Sports Medicine
ADHD	Attention deficit hyperactivity disorder
ADL	Activities of daily living
AHA	American Heart Association
AIMS	Alberta Infant Motor Scales
ANOVA	Analysis of variance
APOE	Apolipoprotein E
ASQ-3	Schedule of Growing Skills-II and the Ages and Stages Questionnaire
AS	Aortic stenosis
ASD	Atrial septal defect
AVSD	Atrioventricular septal defect
BCAS	Boston Circulatory Arrest Study
BDI-2	Battelle Developmental Inventory, Second Edition
BSID	Bayley Scales of Infant and Toddler Development
BSID-II	Bayley Scales of Infant and Toddler Development, Second Edition
BSID-III	Bayley Scales of Infant and Toddler Development, Third Edition
CCF	Congestive cardiac failure
CDC	Centre for Disease Control and Prevention
CDI	Child Development Inventory
CDR	Child Development Review
CHD	Congenital heart disease
Cm	Centimetres
CNP	Cardiac neurodevelopmental programme
CNS	Central nervous system

CPB	Cardiopulmonary bypass
DC	Difficult child
DD	Developmental disorder and disability
DHCA	Deep hypothermic circulatory arrest
DoH	Department of Health
DORV	Double outlet right ventricle
DS	Down syndrome
ECMO	Extracorporeal membrane oxygenation
ENCA	eNews Channel Africa
EI	Early intervention
FITT	Frequency, intensity, type and time
FTT	Failure to thrive
GDP	Gross domestic profit
GMDS-ER	Griffiths Mental Development Scales-Extended Revised
GORD	Gastroesophageal reflux disease
HAZ	Height-for-age z-score
HCAZ	Head circumference-for-age z-score
HIV	Human immunodeficiency virus
HLHS	Hypoplastic left heart syndrome
HRQOL	Health-related quality of life
ICU	Intensive care unit
ICF	International Classification of Functioning, Disability and Health
ICF-CY	International Classification of Functioning, Disability and Health Child and Youth Version
IQ	Intelligence quotient
ISP	Index of social position
Kg	Kilogram

MRI	Magnetic resonance imaging
MSEL	Mullen Scales of Early Learning
NDT	Neurodevelopmental therapy
NHREC	National Human Research Ethics Council of South Africa
OT	Occupational therapy
PCHA	Paediatric Congenital Heart Association
PedsQL™	Paediatric Quality of Life Inventory
PEM	Protein energy malnutrition
PDA	Patent ductus arteriosus
PHTN	Pulmonary arterial hypertension
PS	Pulmonary stenosis
P-CDI	Parent-child dysfunction
PDMD-4	Peabody Development Motor Scales, Second Edition
PT	Physiotherapy
PVL	Periventricular leukomalacia
PSI	Parenting Stress Index
PSI-SF	Parenting Stress Index- Short Form
QOL	Quality of life
RSA	Republic of South Africa
RTHB	Road to Health Booklet (South Africa)
SD	Standard deviation
SES	Socioeconomic status
SA	South Africa
SMS	Short message service
SpO_2	Oxygen saturation
ST	Speech therapy
TAPVR	Total anomalous pulmonary venous return

TAPQOL	Netherlands Organisation for Applied Scientific Research Academic Medical Centre Preschool Children Quality of Life
TB	Tuberculosis
TGA	Transposition of the great arteries
TOF	Tetralogy of Fallot
UK	United Kingdom
UN	United Nations
UNICEF	United Nations International Children's Emergency Fund
US	United States
VAD	Ventricular assist device
VSD	Ventricular septal defect
WAZ	Weight-for-age z-score
WB	World Bank
WHO	World Health Organisation

DEFINITION OF TERMS

Burden of care	Refers to the discomfort experienced by a primary caregiver related to their caregiving role that affects their health, psychosocial wellbeing, financial status and social life (Zarit et al., 1980).
Cardiac neurodevelopmental programmes	Refers to a programme that provides comprehensive and evidence-based neurodevelopmental assessment, second opinions, and consultation and intervention services by a team of specialists (Boston Children's Hospital, 2016).
Congenital heart defect	Refers to a structural abnormality of the heart and/ or the large blood vessels occurring during the early period of foetal life (American Heart Association, 2015).
Congenital heart disease	Refers to the lifelong consequences of being born with a congenital heart defect (Paediatric Congenital Heart Association, 2014).
Early developmental intervention	Refers to educational and neuroprotective strategies aimed at enhancing brain development and optimising developmental and functional outcome. Early educational strategies seek to take advantage of cerebral plasticity, whilst neuroprotective strategies include therapeutic interventions and environmental modifications that promote typical development and prevent disability (Spittle et al., 2015; Bonnier, 2008).

Health-related quality of life	Refers to the perception of the impact of a disease and its treatment on a person's ability to function and derive satisfaction in a variety of aspects of life including the physical, psychological and social domains (Eagleson et al., 2013).
Home programme	Refers to therapeutic activity performed with parental assistance in the home environment and in the context of daily family life, with the goal of achieving desired health outcomes (Novak and Cusick, 2006).
Parenting stress	Refers to the psychological distress experienced by parents in trying to meet the demands of their parenting role (Golfenshtein et al. 2016).

OPERATIONAL DEFINITIONS

Central South Africa	For the purpose of cardiology services in South Africa it refers to the Free State and Northern Cape provinces of South Africa, and the neighbouring country of Lesotho (Hoosen et al., 2010a).
Developmental delay	Refers to a child whose developmental maturation or mental and/or physical skills are not consistent with the typical timeframe (Marino et al., 2012).
Developmental disorder and disability	Refers to the presence of a neurocognitive or neurobehavioral abnormality or limitation, psychosocial maladjustment or physical limitation (Marino et al., 2012).

Young child	For the purpose of this study, a young child refers to a child aged one-month to three-and-a-half years (Marino et al., 2012).

CHAPTER 1

INTRODUCTION

1.1 Congenital heart disease: A global perspective

Congenital heart defects are the most common structural birth abnormality affecting children (AHA, 2015), as well as being the most commonly diagnosed chronic health condition in infancy (CDC, 2015). Congenital heart defects result from the complex interactions of multiple environmental and genetic factors, and, in many cases, the exact cause remains undetermined (Bernier et al., 2010).

The current incidence of congenital heart disease (CHD) is similar across the world, and is estimated to range between eight and twelve per 1000 live births (Hoffman, 2013). This equates to approximately one percent of all children being born with a heart defect (Yildiz et al., 2009). Geographical location, genetics, ethnicity and environmental factors have not been found to have a significant impact on incidence (AHA, 2015; PCHA, 2014; Zühlke et al., 2013). The incidence of CHD appears to be on the rise globally (CDC, 2015; Bernier et al., 2010). Three per 1000 children born with CHD will require catheter-based or surgical intervention early on in life (Marino et al., 2012; *The Lancet*, 2012; Gruber and Epstein, 2004; Hoffman and Kaplan, 2002).

Diagnostic, medical and surgical advances over the past few decades have resulted in survival becoming the expected outcome for most children born with CHD (Rappaport 2015; PCHA, 2014). Most children with complex CHD awaiting heart transplantation require mechanical ventilation and/or mechanical circulatory support as a bridge to myocardial recovery and transplantation. Mechanical circulatory support technologies including extracorporeal membrane oxygenation (ECMO) and ventricular assist devices (VADs), is a

rapidly growing field, and the use of these technologies is becoming more popular for children with end stage heart disease due to the limited donor pool of organs (Wilmot et al., 2013; Gazit el al., 2010). A growing number of children are being supported as more centres in developed countries adopt these mechanical circulatory support technologies (Deshpande et al. 2016). Today, approximately 85% of children born with CHD survive and are expected to live into adulthood (Eagleson et al., 2013; *The Lancet*, 2012; Hoosen et al., 2010b). Improved survival has seen CHD become one of the fastest growing chronic health conditions in childhood (Lee et al., 2007; Mussatto, 2006). As a result, the focus has shifted beyond survival toward looking at longer-term outcomes and morbidities including growth, development, health-related quality of life (HRQOL), as well as the psychosocial functioning of both the child and family (Eagleson et al., 2013; Marino, 2013; Marino et al. 2012; Marino et al., 2010; Baker, 2008).

Children surviving CHD often require ongoing medical care over their lifetime (Nolte and McKee, 2008). Many children face an uncertain future requiring long-term follow-up, multiple cardiac interventions, the chronic use of medication and the possibility of permanent disability (Mussatto, 2006). Increased focus on long-term outcomes is continuing to provide convincing evidence that CHD survivors are at considerably higher risk for developmental delay and developmental disorders and disabilities (DD) than the general population (Marino et al., 2012). Physical and psychosocial dysfunction may in turn negatively affect the child's HRQOL (Marino et al., 2016).

In the light of the developmental findings in the CHD population, the paediatric cardiac community has been actively searching for ways in which to improve neurodevelopmental outcomes. One of the ways is through advocacy for neurodevelopmental screening and evaluation as part of standard cardiac care. The American Heart Association (AHA) and the American Academy of Paediatrics (AAP) released a scientific statement in 2012 strongly recommending the implementation of routine cardiac neurodevelopmental follow-up (Marino et al., 2012).

Since the publication of these evaluation and management guidelines by Marino et al. (2012) just over four years ago several cardiac neurodevelopmental programmes (CNPs) have been initiated at cardiac centres, mainly across the United States (US). Only a few countries

outside of the US have initiated similar programmes, including Canada, Australia, Germany, Japan and New Zealand (Gaynor et al., 2015). Existing CNPs tend to be managed by interdisciplinary teams collaborating with a psychologist or developmental paediatrician. Some CNPs do include the services of allied health professionals including physiotherapists, occupational therapists, speech therapists and dieticians (Mahle, 2015; Brosig et al., 2014). Today, dedicated CNPs are considered the benchmark of a quality cardiac service (Mahle, 2015; Brosig et al., 2014). CNPs are a relatively new component of cardiac care, resulting in limited scientific evidence being available on the best mode of programme delivery, or the success and clinical value of these programmes in addressing the developmental needs of children with CHD (Brosig et al., 2014).

Long et al. (2015), Steiber et al. (2012) and Brosig Soto et al. (2011) have noted several challenges in implementing both hospital-based and home-based developmental intervention programmes in this population. Challenges included distance to travel to cardiac centres, lack of motivation on the part of families to attend therapy sessions, and a lack of adherence to prescribed home programmes. Valid questions have been raised about the feasibility and best model for providing early developmental intervention in the CHD population, indicating the need for further investigation.

Many parents find raising a child with CHD challenging (Brosig et al., 2007; Mussatto, 2006). The increased burden of caring for a child with a chronic health condition places parents at risk of experiencing ongoing stress and psychosocial morbidity, which may later manifest as anxiety or depression (Bruce et al., 2014; Solberg et al., 2011; Vrijmoet-Wiersma et al., 2009). Furthermore, many families experience considerable financial strain because of the burden of care preventing gainful employment and the high cost of ongoing treatment. The financial strain further contributes to parenting stress (Grønning Dale et al., 2013; Harvey et al., 2013; Fonseca et al., 2012; Soulvie et al., 2012; Connor et al., 2010; Lawoko and Soares, 2006; Mussatto, 2006). This has resulted in the psychosocial functioning of the family becoming an important outcome measure of successful treatment. Routine and regular screening of families for psychosocial risk is advocated for as part of standard cardiac care so as to identify families in need of additional support (Hearps et al., 2014; Mussatto, 2006).

In sum, limited information is currently available on the longer-term outcomes, especially for young children living with CHD, even in the developed world. For this reason the cardiac community at large has identified growth, development and HRQOL outcomes of the child, as well as the psychosocial outcomes of both the child and family as key focus areas for research endeavours going forward.

1.2 Congenital heart disease: An African perspective

Despite the incidence of CHD being described in the literature as being similar across the world, South Africa (SA) has one of the highest incidences of CHD in the world due to the high fertility rate and greater number of children born per female member of the population (Lee, 2014; Hoffman, 2013; Zühlke et al., 2013; Hoosen et al., 2010a). The SA population continues to grow and the paediatric population is large, with nearly 30% of the country's population under the age of 14 years (Zühlke et al., 2013; Statistics South Africa, 2012; Hoosen et al., 2011). Studies are also showing the incidence of CHD, especially milder forms, to be on the rise in SA (CDC, 2015; Reuters South Africa, 2015). Figure 1.1 provides a graphic representation of the total number of children born with CHD per continent (Hoffman, 2013).

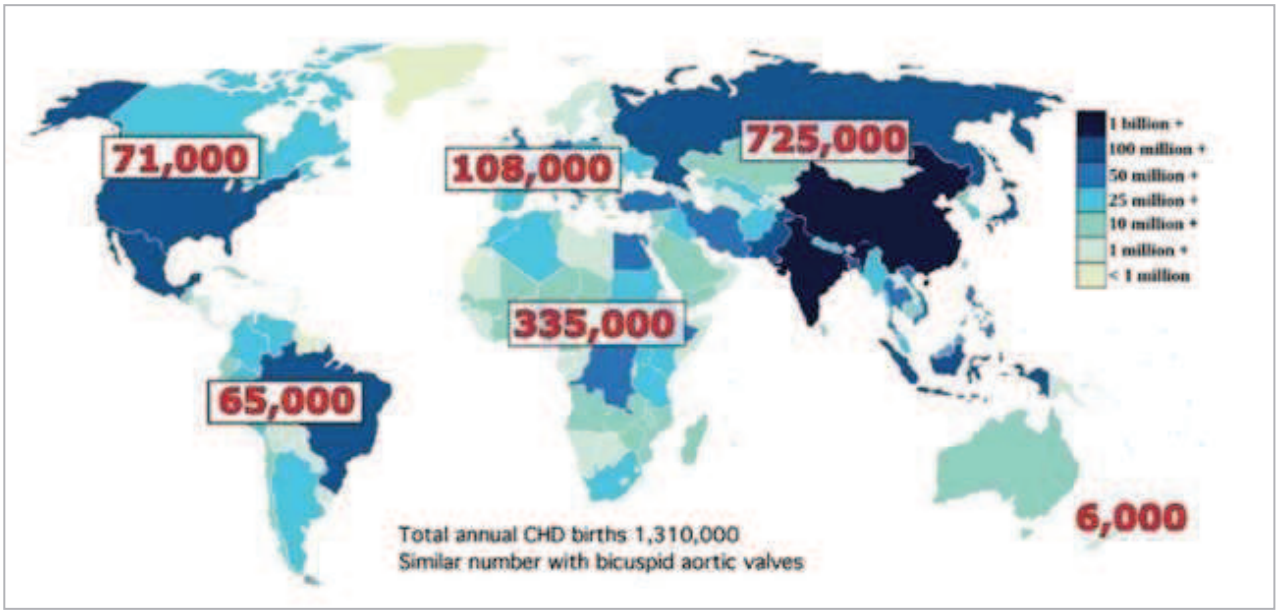

Figure 1.1 Total annual births of children with CHD per continent (Hoffman, 2013, p 142).

Across Africa there is a considerable burden of communicable diseases such as tuberculosis (TB), human immunodeficiency virus (HIV) and diarrhoeal disease, as well as childhood malnutrition (Bradshaw et al., 2003). Healthcare services and funding have been prioritised to meet this considerable burden (Hoosen et al., 2010b; Bradshaw et al., 2003). CHD only ranks eighth on the list of leading causes of under-five mortality in SA, perhaps putting into perspective the lack of prioritisation of non-communicable diseases such as CHD on the African continent (Hoosen et al., 2010b; Bradshaw et al., 2003). African countries are now being faced with a growing double burden of disease, with non-communicable diseases such as cardiac disease becoming a growing cause of morbidity (Kengne and Mayosi, 2013; Mbewu, 2009).

CHD continues to have a poor prognosis in SA, and remains a considerable cause of mortality in infants and young children (Zühlke et al., 2013; Hoosen et al., 2011; Bernier et al., 2010). Despite a large portion of the gross domestic product (GDP) being allocated to healthcare in SA, compared to other middle-income countries, health outcomes remain poor, and there is a considerable disparity between health services provided in the private sector compared to the public sector (Edmeston and Francis, 2014; Hoosen et al., 2010b). Despite huge strides being made in the diagnosis and treatment of CHD in the developed world, similar successes have not been replicated in Africa (Zühlke et al., 2013).

Based on current population statistics it can estimated that nearly 12 100 children are born with CHD in SA each year (Statistics South Africa, 2014). Of these children, 85% are dependent on the public health sector for their cardiac care (Edmeston and Francis, 2014; Hoosen et al., 2010a). Caring for children with CHD is complex and very resource-intensive (CDC, 2015), and access to care is not equal for all children with CHD, especially for those living in developing countries (Bernier et al., 2010). Cardiac services are limited in Africa and are less accessible to patients than is the case in developed countries (Lee, 2014; Kinsley, 2012; Kinsley et al., 2011). Figure 1.2 highlights the lack of well-established independent cardiac programmes in Africa, with the only well-established programmes running in SA, Sudan and Egypt (Zühlke et al., 2013).

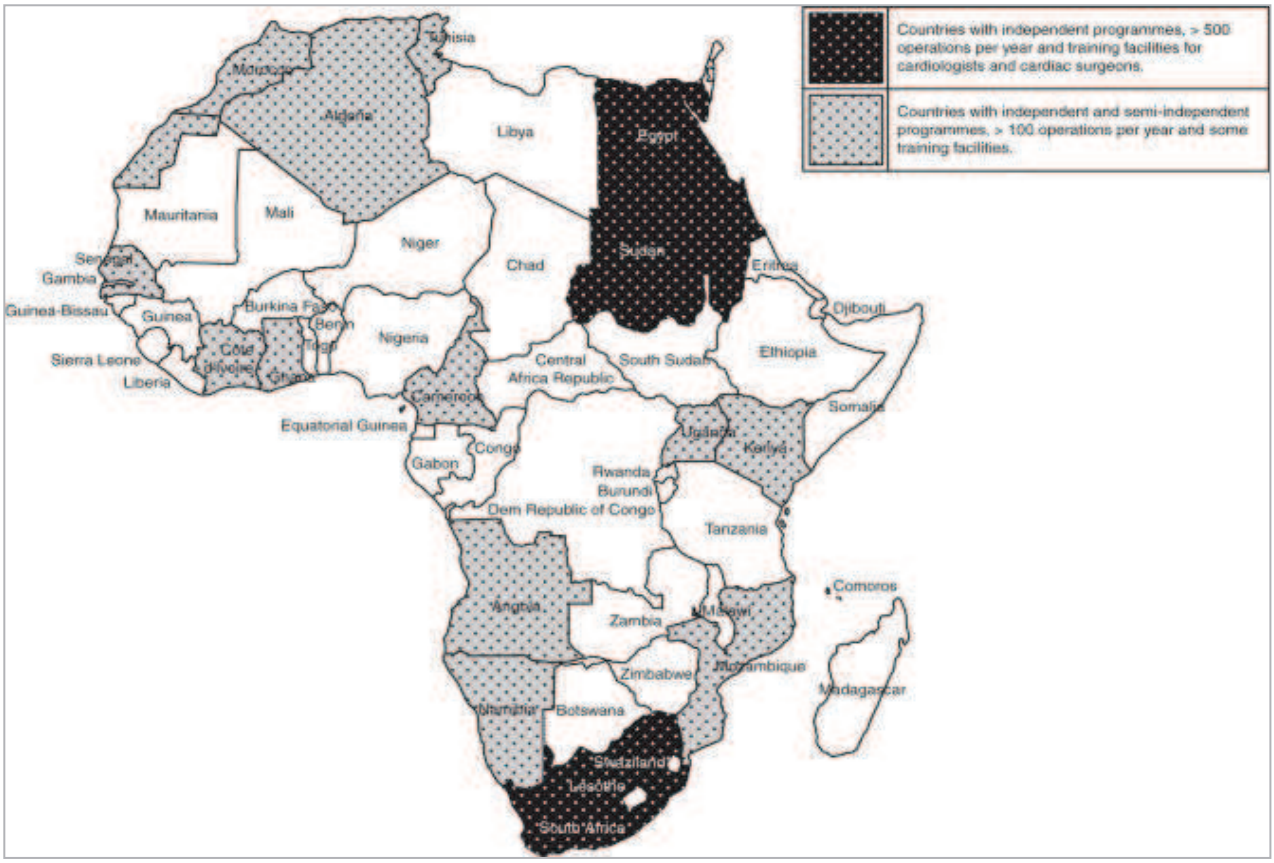

Figure 1.2 African countries with cardiac programmes (Zühlke et al., 2013, p 6)

With the large number of children born annually with CHD, requiring specialist care, there is a significant demand for cardiac services, especially in the public health sector in SA, which cannot be met despite the country having relatively well-established cardiac services. In addition, children from surrounding countries are also referred to SA for treatment, further increasing the demand for services (Lee, 2014; Hoosen et al., 2010a). There are only five centres that offer comprehensive cardiac care to children and their families in the public health sector in SA, and these centres are spread over a wide geographical location (Hoosen et al., 2010a; Robertson, 2006). High patient numbers, a shortage of skilled human resources (including cardiologists and cardiothoracic surgeons), inadequate infrastructure and a shortage of intensive care unit (ICU) beds result in the overburdening of cardiac services in the public health sector. The direct result being that cardiac centres are unable to provide adequate services to the paediatric cardiac population of SA (Van Deventer et al., 2015; Lee, 2014; Zühlke, 2013; Hoosen et al., 2011; Hoosen et al., 2010a; Hoosen 2010b; Robertson, 2006). Currently it is suggested that about 60% of children requiring cardiac services in SA are not being diagnosed or treated (Reuters South Africa, 2015).

Of the children diagnosed with CHD in SA, approximately 50% will require invasive diagnostic procedures and 40% will require open-heart surgery (Hoosen et al., 2010a; Hoosen et al., 2010b). Based on available data, only around 800 cardiac surgeries are performed on children in the public health sector and 570 in the private health sector in SA each year. This represents just over a third of the estimated 4 000 children requiring cardiac surgery each year in the country (Hoosen et al., 2010a; Hoosen et al., 2010b).

Children with CHD in Africa have a dramatically different prognosis and outcome when compared with children living in the developed world (Binagwaho et al., 2013; Zühlke et al., 2013). Mortality due to CHD remains higher in developing countries compared to developed countries (Lee, 2014). It is also estimated that only between 70 and 80% of children born with CHD in SA, who receive optimal cardiac services, will survive into adulthood (Gersh, 2011). Children with complex CHD and those awaiting heart transplantation in SA may have access to mechanical ventilatory support, but mechanical circulatory support technologies such as ECMO and VADs are relatively new in SA. Few children, and only those who are critically ill, and can no longer wait for a donor, have access to these technologies as a bridge to transplantation due to the cost (Carte Blanche, 2017; Hoosen et al., 2010a). Children also present with unfavourable health conditions pre-operatively including low birth weight, malnutrition and HIV co-infection, which further complicate treatment and outcome (Lee, 2014; Kinsley et al., 2011; Hoosen et al., 2010b).

The consequences and cost of untreated CHD to the country is considerable. For some children not managed early enough, their defects become inoperable resulting in poor health outcomes (Kinsley et al., 2011). Recurrent hospitalisation to manage the resulting complications, which may include stroke, pulmonary arterial hypertension (PHTN) and congestive cardiac failure (CCF), increase the emotional and financial burden on families (Lee, 2014; Hoosen et al., 2011; Hoosen et al., 2010a).

Continuity of care also remains a problem in Africa. There is a high loss to follow-up post-cardiac surgery and many patients fail to receive the ongoing care they require. The loss to follow-up for cardiac care on the continent is estimated to be between 30 and 40% (Lee, 2014; Mocumbi et al., 2011; Tantchou Tchoumi et al., 2011).

In sum, despite the global focus on longer-term outcomes, little is known about the outcomes of children living with CHD and their families in Africa and more specifically SA. Growth, development and HRQOL outcomes of young children with CHD in SA have not been determined. Parenting stress and the burden of caring for a child with CHD in SA is also unknown.

1.3. Problem statement

Low and middle-income countries bear 80% of the burden of cardiovascular disease in the world (Binagwaho et al., 2013). Despite the considerable burden of cardiovascular disease in Africa, socioeconomic circumstances and the health needs of the continent have resulted in little cardiovascular research being done in Africa (Edwin et al., 2011; Hoosen et al., 2010b). Rosmarakis et al. (2005) investigated global cardiovascular research outputs and found that Africa's contribution to the number of published scientific articles on cardiovascular disease was the lowest of all continents at only 0.3%.

Clinical cardiovascular research is required to address problems of importance in the African context (Gersh, 2011). The burden of disease and health outcomes of children with CHD in SA need to be determined (Kengne and Mayosi, 2013; Zühlke et al., 2013; Kinsley et al., 2011; Hoosen et al., 2010a; Hoosen et al., 2010b). In addition, SA needs population-based research to determine the services required to address the burden of cardiovascular disease in the country (Smit, 2015).

The Republic of South Africa Department of Health (RSA-DoH) has renewed its commitment to improving access to care, ensuring the early identification and appropriate management of CHD (Lee, 2014; Bamford, 2013). However, there are considerable challenges in meeting this commitment. Finding innovative ways of delivering quality cardiac services to children within a human resource, infrastructure and financially-constrained environment should be a healthcare priority (Zühlke, 2013). In addition, research in Africa should focus on decreasing morbidity and improving the HRQOL and psychosocial outcomes of children living with CHD, and their families (Binagwaho et al., 2013; Zühlke, 2013).

The growth, developmental and HRQOL outcomes of young children living with CHD in Africa have not been determined. The burden of care and psychosocial outcomes of parents caring for these children is also unknown. Without knowing these outcomes, it is impossible to plan for, and provide suitable interventions.

The feasibility of implementing regular cardiac neurodevelopmental follow-up for children with CHD in Africa has not been investigated, and there is no documented record of any CNPs or early cardiac developmental intervention programmes running at any of the cardiac centres on the African continent at this point in time.

The best mode of providing early developmental intervention to children with CHD at risk of, or presenting with developmental delays in SA needs to be investigated, keeping in mind that the South African public health system follows a community-based approach. Therefore possible ways of providing community-based and home-based intervention services need to be explored (Van Deventer et al., 2015).

1.4 Research questions

The following research questions were asked in this study:

What are the pre-cardiac intervention developmental status, HRQOL and burden of care of young children living with CHD in central SA?

What are the three-month and six-month post-cardiac intervention developmental status, HRQOL and burden of care of young children living with CHD in central SA?

What type of home-based, caregiver-driven developmental stimulation programme would be best suited to address the specific developmental needs of young children living with CHD, and their caregivers, in central SA?

1.5 Aims

The aims of this study were threefold:

The first aim was to determine the pre-cardiac intervention developmental status, HRQOL and burden of care of young children living with CHD in central SA.

The second aim was to determine the three-month and six-month post-cardiac intervention developmental status, HRQOL and burden of care of young children living with CHD in central SA.

The third aim was to identify the developmental needs of young children living with CHD in central SA, and to develop a validated, home-based, caregiver-driven developmental stimulation programme aimed at addressing their specific needs.

1.6 Objectives

The objectives for the three phases of the study are presented under main and secondary objectives.

1.6.1 Main objectives

The main objectives for each of the three phases of the study are stated below:

Phase I

To establish the pre-cardiac intervention (baseline) growth, development and cardiovascular status of children living with CHD in central SA.

To establish the pre-cardiac (baseline) intervention HRQOL of children living with CHD in central SA.

To establish the pre-cardiac intervention (baseline) levels of parenting stress and the burden of care experienced by parents of children living with CHD in central SA.

Phase II

To establish the three-month and six-month post-cardiac intervention growth, development and cardiovascular status of children living with CHD in central SA.

To establish the three-month and six-month post-cardiac intervention HRQOL of children living with CHD in central SA.

To establish the three-month and six-month post-cardiac intervention levels of parenting stress and the burden of care experienced by parents of children living with CHD in central SA.

To compare growth, development and HRQOL of children living with CHD, and parenting stress over time, from pre-cardiac intervention up until the six-month post-cardiac intervention.

Phase III

To establish the nature and severity of the developmental challenges faced by young children living with CHD in central SA.

1.6.2 Secondary objectives

Phase II

To compare the growth, development, HRQOL and parenting stress of children with CHD with Down Syndrome (DS) to those with CHD without DS over time, from pre-cardiac intervention up until the six-month post-cardiac intervention.

To compare growth, development, HRQOL and parenting stress of children with cyanotic heart defects with those with acyanotic heart, from pre-cardiac intervention up until the six-month post-cardiac intervention.

To determine the association between multiple variables and development, HRQOL and parenting stress outcomes of the children in the current study sample.

Phase III

To develop and validate a home-based, caregiver-driven developmental stimulation programme addressing the specific developmental needs of young children with CHD.

1.7 Significance of the study

This is the first study investigating the developmental outcomes of young children undergoing cardiac intervention on the African continent. The determination of developmental outcomes using the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) was considered the most important aim of this study, as it would allow for comparison of developmental outcomes of SA children living with CHD with other children with CHD in developed countries. Furthermore, determining growth and HRQOL outcomes will provide valuable insights into the growth, health and wellbeing of children living with CHD in SA. The study also serves to identify variables associated with development and HRQOL outcomes in young children living with CHD in SA.

Identification of specific developmental concerns assisted in the development of a home-based, parent-driven developmental home activity programme that specifically met the needs of young children living with CHD in SA. Apart from this, the home-based developmental stimulation programme will be the first documented programme providing a comprehensive description of the rationale, development, programme content and treatment dosage for children living with CHD worldwide (other studies to date have not provided specific information on home programme development and content). The programme can be issued to parents as a resource tool in order to support and optimise developmental outcome as part of a CNP.

The study followed-up young children living with CHD and their families from just before cardiac intervention, over a period of six months post-cardiac intervention. This allowed for invaluable insights into the possible feasibility and potential challenges of implementing CNPs in the South African setting. Recommendations can be provided to stakeholders in

both SA and in Africa in this regard.

Establishing the levels of parenting stress and the burden of care was considered an extremely important outcome in this study. In following a family-centred approach to cardiac care, it is deemed of the utmost important to put strategies in place to better support parents in their role of caring for a child with CHD.

1.8 Organisation of the thesis

The thesis is organised under the following chapters:

Chapter 1: Introduction

Chapter 2: Literature review

Chapter 3: Measurement tools and pilot study

Chapter 4: Methods Phase I and Phase II

Chapter 5: Results Phase I and Phase II

Chapter 6: Discussion of the results of Phase I and II

Chapter 7: Phase III: Development and validation of the developmental home activity programme

Chapter 8: Conclusion

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

This chapter will provide an overview of CHD in children, with the emphasis on CHD in infants, toddlers and pre-schoolers. The chapter is divided into six sections delineating the focus areas of this study. Due to the participant profile in the current study outcomes for children with CHD with genetic abnormalities will focus on DS.

Section 2.2 will provide a brief overview of CHD, including the classification thereof according to the nature of the defect and medical severity. The medical and surgical management of CHD will also be indicated.

Section 2.3 will present relevant literature regarding the impact of CHD on the developing brain, identify risk factors for adverse neurodevelopmental outcome and describe patterns of developmental delay and impairment found in children with CHD. Relevant findings from neurodevelopmental outcome studies published to date will also be highlighted. Recommendations regarding cardiac neurodevelopmental follow-up and early developmental intervention in improving neurodevelopmental outcome will be outlined for further discussion in Chapter 7.

Section 2.4 will review the reasons for the high occurrence of malnutrition and growth failure in children with CHD, with special attention being paid to the impact of growth failure on neurodevelopmental outcome in this population.

Section 2.5 will present current literature on HRQOL outcomes in children with CHD, and review factors that adversely affect HRQOL in this population.

The last two sections will describe the cost of CHD to families. The burden of CHD for families may be both psychosocial and financial in nature. Section 2.6 will review stressors associated with parenting and caring for a child with a chronic health condition, while Section 2.7 will describe the financial burden of care.

Articles for this literature review were sourced using the EBSCO host platform, the following databases and search engines were used: CINAHL with full text, Medline with full text, PsycINFO, PEDro, Cochrane Library, Africa-wide Information, BMJ journals online, Academic Search Complete, GOOGLE scholar, PubMed, African Journals Online and Science Direct. Key words used in searches in combination with congenital heart disease or congenital heart defect included neurodevelopmental outcome, developmental outcome, cardiac neurodevelopmental follow-up, neurodevelopmental risk, early developmental intervention, health-related quality of life, quality of life, growth failure and malnutrition, Down syndrome, parenting stress, financial cost to families and burden of care. The search period extend up to and including articles published in July 2016.

2.2. CONGENITAL HEART DISEASE IN CHILDREN

2.2.1 Risk factors for congenital heart disease

CHD is attributed to multifactorial aetiologies arising from interactions between multiple genes and environmental factors (Chaix et al., 2016). Genetic causes can be identified in fewer than 20% of cases of CHD (Fung et al., 2013), while around 30% of congenital heart defects are attributable to identifiable, non-inherited causes including maternal low socioeconomic status (SES), stress, illness, nutritional deficiencies, therapeutic and non-therapeutic drug use and chemical exposure during early foetal life (Fung et al., 2013; Patel and Burns, 2013; Jenkins et al., 2007). However, in many cases the exact cause remains unknown (CDC, 2015).

2.2.2 Prevalence and survival

The prevalence of CHD is estimated to be around nine per 1000 live births (Marino et al., 2012). Most children born with CHD today will survive into adulthood. Survival rates do however vary according to disease severity. According to Marino et al. (2012) the long-term survival rate for children with simple or mild forms of CHD (valve disease, and atrial and ventricular septal defects) is estimated to be 95%, 90% for children with CHD of moderate severity (coarctation of the aorta, atrioventricular septal defect, ventricular septal defect with comorbidities, tetralogy of Fallot), and 80% for children with complex or severe forms of CHD (single ventricle, truncus arteriosus, complex transposition of the great arteries). Even though complex types of CHD such as hypoplastic left heart syndrome (HLHS) have lower survival rates, the overall survival rates for even the most complex cardiac defects have improved.

2.2.3 Classification of congenital heart defects

2.2.3.1 Classification based on the nature of the defect

CHD can be classified according to the presence or absence of cyanosis. Acyanotic lesions are characterised by a normal arterial blood oxygen saturation and a pink skin colour. Cyanotic lesions on the other hand are characterised by reduced levels of oxygen in the arterial blood and a bluish skin discolouration (Nousi and Christou, 2010).

The most common acyanotic heart defects are ventricular septal defects (VSD) and artrioventricular septal defects (AVSD) (30-50%), patent ductus arteriosus (PDA) (10%), atrial septal defects (ASD) (7-10%), pulmonary valve stenosis (PS) (7%), aortic valve stenosis (AS) (6%) and coarctation of the aorta (6%) (Hanson, 2015; Nousi and Christou, 2010). While the most common cyanotic heart defects include tetralogy of Fallot (TOF) (5%) and transposition of the great arteries (TGA) (5%) and double outlet right ventricle (DORV) (5%). Several other rare and complex cardiac defects that can occur include hypoplastic left heart syndrome (HLHS), truncus arteriosus, tricuspid valve atresia, interrupted aortic arch and total anomalous pulmonary venous return (TAPVR)(Hanson, 2015; Nousi and Christou, 2010). Congenital heart defects occur in between 41 to 56% of children with DS with AVSDs being the most common defect (Alsaied et al., 2016; Elmagrpy et al., 2011; Van Gameren-Oosterom et al., 2011; Visootsak et al., 2011).

The classification of CHD according to the nature of the defect is presented in Appendix I.

2.2.3.2 Classification based on the medical severity

Disease severity may affect prognosis and outcome. Despite the importance of cardiologists being able to identify the severity of the defect, no universally agreed upon classification system exists (Macran et al., 2006). A medical severity rating scale for CHD, the Cardiologist's Perception of Medical Severity Scale (DeMaso et al., 1991) has been used in studies by Uzark et al. (2003) and Yildiz et al. (2009) to rate disease severity.

The rating system according to the Cardiologist's Perception of Medical Severity Scale is presented in Appendix II.

2.2.4 Management of congenital heart disease

Treatment is guided largely by the nature and severity of the defect, as well as the child's age. In some cases, minor defects resolve spontaneously and require no intervention. In other cases where the defect is more significant, management may include supportive medical care in the form of the administration of cardio-active drugs, interventional cardiac catheterisation or cardiac surgery (AHA, 2015; Howell and Tapley, 2012; Lee et al., 2007). Approximately 25 to 30% of children born with CHD will require surgery which may be corrective or palliative (Owen et al., 2011).

2.2.5 Summary

Congenital heart defects are the most common birth abnormality, with a prevalence of around nine per 1000 live births. It is estimated that around 85% of children born with a congenital heart defect will survive into adulthood. The cause of CHD in many cases remains unknown, but the interactions between multiple genetic and environmental factors are believed to be causative. Management of CHD is determined by the nature and severity of the cardiac defect, and may require a combination of medical, interventional cardiology and cardiac surgery interventions to palliate or repair the defect.

2.3 NEURODEVELOPMENTAL OUTCOME IN CHILDREN WITH CONGENITAL HEART DISEASE

2.3.1 Introduction

Over recent decades advances in medical management and surgical techniques have significantly reduced mortality in children born with CHD (Gaynor et al., 2015; Marino et al., 2012; Snookes et al., 2010). More children at high-risk of neurodevelopmental morbidity are now undergoing cardiac surgery than ever before, and are surviving. This has resulted in a growing population of CHD survivors who are presenting with neurodevelopmental problems (Gaynor et al., 2015). As a result, the focus has shifted to these longer-term outcomes (Naguib et al., 2015).

Brain injury and subsequent developmental disability is the most common and potentially devastating long-term complication of CHD (Gaynor et al., 2015; Snookes et al., 2010). Impairments include developmental delays, difficulty in school, and challenges in living independently (Rollins and Newburger, 2014).

Children with CHD are at risk of neurodisability regardless of the severity of their CHD (Mussatto et al., 2014; Snookes et al., 2010). It is well established that children with CHD experience a higher prevalence of developmental delay and disability than typically developing healthy children (Mussatto et al., 2015; Martinez-Biarge et al., 2013). For many children and their families the neurodevelopmental burden of disease is far greater than the daily impact of the CHD itself (Wernovsky, 2008).

Children with CHD typically show areas of strength and weakness in their development, a so-called unique “developmental signature” that changes with developmental age (Brosig et al., 2014). The extent of the developmental deficits tend to become more apparent over time and with age, becoming more pronounced as the child attempts to master tasks that are more complex. These deficits do not disappear upon transition into adolescence and later into adulthood (Wilson et al., 2015). Significant variation is seen in developmental outcome; even amongst children with the same cardiac defect (Gaynor et al., 2014; Sananes et al., 2012; Acton et al., 2011), suggesting that patient-specific factors may play an important role

in determining central nervous system (CNS) injury and therefore neurodevelopmental outcome (Mussatto et al., 2015; Gaynor et al., 2014; Sananes et al., 2012).

The cause of neurodevelopmental disability in children with CHD is most likely multifactorial, but the precise role of specific medical, surgical, and sociodemographic variables is not yet fully understood (Medoff-Cooper et al., 2016; Ravishankar et al., 2013). Various patient-specific and management factors have the potential to interact during the pre-operative, peri-operative, and post-operative periods, manifesting as a spectrum of developmental difficulties in children with CHD (Chock et al., 2012; Long et al., 2012b; Owen et al., 2011; Joynt et al., 2009).

In the light of the aforementioned, neurodevelopment now ranks amongst the most important outcomes being scrutinised in children with CHD (Goldberg et al., 2011; Dittrich et al., 2003). Research is becoming more focused on defining the impact of CHD on brain development, minimising postnatal brain injury, and improving long-term neurodevelopmental outcomes for survivors (Donofrio and Massaro, 2010). This creates a new challenge for healthcare professionals of coming to understand the neurobehavioural profile of these children and being able to respond to this with the provision of the necessary early intervention (EI), psychological and educational services needed to support these children's optimal development and long-term outcome (Gerdes and Flynn, 2010).

2.3.2 Brain abnormalities associated with congenital heart disease

Brain injury is a potentially devastating complication of CHD (Gunn et al., 2012). CHD can affect the brain in several different ways (Rollins and Newburger, 2014; Goldberg et al., 2011). The structural differences in the brains of children with CHD can be divided into two categories: abnormalities of brain development and acquired brain injury (Martinez-Biarge et al., 2013). In addition to this, genetic susceptibility may also play a role in predisposing the brain to injury in children with CHD (Homsy et al., 2015).

The mechanisms contributing to CNS injury in children with CHD are complex and multifactorial (Albers et al., 2010). Both pre-existing and acquired brain injury have been associated with poorer neurodevelopmental outcomes (Long et al., 2011).

The persistence of poor neurodevelopmental outcome in some children despite the significant improvements in medical and surgical management may indicate the important impact abnormal brain development may have in determining neurodevelopmental outcome in children with CHD (Gaynor et al., 2015).

2.3.2.1 Genetic susceptibility

Scientists at the Harvard Medical School have found a link between a set of gene mutations in the development of CHD and various other neurodevelopmental abnormalities. Homsy et al. (2015) found that children with both CHD and other neurodevelopmental disorders have a much higher burden of damaging *de novo* gene mutations, particularly in genes that play an important role in the development of both the heart and brain. The risk of developing neurodevelopmental disabilities in children with CHD is considered to be extremely high when these specific gene mutations are present. Thus, there is also an increased incidence of structural brain abnormalities in infants with CHD (Rollins and Newburger, 2014; Long et al., 2011).

In addition to this, children carrying the epsilon2 version of the apolipoprotein E (APOE) are likely to have a worse neurodevelopmental outcome after undergoing cardiac surgery than those children who do not possess the gene variant. The epsilon2 gene variant decreases the ability of neurons to repair themselves after brain ischaemia and traumatic brain damage. Genetic variants that decrease the brain's resilience and impair neuronal repair after injury are to be considered an important risk factor for developmental delay and developmental disorder or disability (DD) following cardiac surgery in infants (Gaynor et al., 2014; Fuller et al., 2009).

2.3.2.2 Structural differences in the brain

There is a growing body of evidence to suggest that many children with CHD have abnormal or delayed brain development, potentially making them more vulnerable to neurologic insult (Albers et al., 2010). Abnormal blood flow may occur in the brain of a foetus and infant with CHD, reducing the volume of blood reaching the brain or the oxygen content of the blood (Brosig et al., 2014). Reduced blood flow and oxygen content may retard brain maturation

(Gaynor et al., 2015; Brosig et al., 2014; Rollins and Newburger, 2014; Donofrio et al., 2011; Goldberg et al., 2011), resulting in cerebral hypoxic ischaemia and metabolic acidosis which may give rise to haemorrhaging (intraventricular, parenchymal or subdural), periventricular leukomalacia (PVL) or stroke (Marino, 2013; Tabbutt et al., 2012; Donofrio et al., 2011; Owen et al., 2011).

Magnetic resonance imaging (MRI) studies have shown smaller brain volume, decreased cerebral blood flow and abnormal brain metabolism in infants with CHD (Gaynor et al., 2015; Brosig et al., 2014; Martinez-Biarge et al., 2013; Tabbutt et al., 2012). Brain development has also been found to be slower in children with cyanotic types compared to acyanotic types of CHD (Abdel Raheem and Mohamed, 2012).

2.3.2.3 Acquired brain injury

Beyond these structural differences, infants with CHD are also at high-risk for acquired brain injury (Martinez-Biarge et al., 2013). Injury may be caused by a combination of pre-operative, peri-operative and post-operative factors (Hövels-Gürich et al., 2006). It is suggested that brain injury occurs in approximately 26% of infants with CHD before cardiac surgery and new brain injury occurs in around 44% of infants after undergoing cardiac surgery (Beca et al., 2013). White matter injury is the most common form of brain injury both before and after cardiac surgery (Beca et al., 2013). The risk of brain injury increases with the severity of the defect and the complexity of the surgery required (Snookes et al., 2010).

Altered brain development may increase the vulnerability of the neonatal and infant brain to injury, subsequently increasing the risk of white matter injury as a result of haemodynamic instability and changes in cerebral perfusion and oxygenation (Gaynor et al., 2015; Gunn et al., 2012; Long et al., 2011; Von Rhein et al., 2011; Snookes et al., 2010). Brain injury may result from hypo-perfusion, cerebral venous thrombosis, thromboembolism and infarction, which may be related to the cardiac defect itself, or to the procedures required to repair or palliate the defect (Albers et al., 2010; Dittrich et al., 2003).

In addition, brain immaturity increases the risk of brain injury occurring with stressors such as labour, haemodynamic instability or infection (Rollins and Newburger, 2014; Owen et al.,

2011). The pattern of brain injury seen in a term newborns with CHD is similar to that seen in preterm neonates (Brosig et al., 2014; Martinez-Biarge et al., 2013). In term newborns with CHD, brain maturity may be delayed with as much as a month (Rollins and Newburger, 2014).

Apart from brain maturity, white matter injury is also associated with longer durations of cardiopulmonary bypass (CPB) and the use of deep hypothermic circulatory arrest (DHCA) (Gaynor et al., 2015; Beca et al., 2013). White matter injury can impair both motor and cognitive function, which in turn will negatively affect development and learning (Rollins and Newburger, 2014).

Haemorrhage and stroke occur less frequently, with PVL and stroke occurring in between 23 and 48% of children with CHD, whilst haemorrhages occur in between 7 and 54% of children with CHD (Tabbutt et al., 2012). Davidson et al. (2015) reported that strokes occur secondary to hypoxic or ischaemic damage during CPB in children with complex CHD. Some types of CHD are also more likely to cause blood clot formation. These blood clots may travel to the brain, obstructing blood vessels, causing a stroke. Both cardiac surgery and cardiac catheterisations can be complicated by a stroke (Rollins and Newburger, 2014). Domi et al. (2008) investigated the frequency and predictors of vaso-occlusive strokes in children undergoing cardiac surgery. They found one in 185 children undergoing cardiac surgery suffered a stroke (risk of 5.4 strokes per 1000 children). The study also revealed that older age at the time of surgery, longer durations of CPB, longer post-operative hospital length of stay and reoperation to be associated with stroke.

2.3.3 Abnormal neurological examinations

Abnormal neurological examinations have been reported in between 36 and 56% of newborns and infants with CHD (Marino et al., 2012; Tabbutt et al., 2012; Donofrio et al., 2011). Neurological abnormalities include hypotonia, hypertonia, jitteriness, motor asymmetry, and poor sucking reflexes (Marino et al., 2012; Donofrio et al., 2011; Donofrio and Massaro, 2010). Of the aforementioned, hypotonia is by far the most frequently reported neurological abnormality in children with CHD (Lata et al., 2015; Majnemer et al., 2009; Limperopoulos et al., 2000). Newborns and infants may exhibit profound hypotonia post-

cardiac surgery, especially in cases of prolonged post-operative sedation and mechanical ventilation (Long et al., 2011). Abnormal neuromotor findings are associated with adverse neurodevelopmental outcomes (Chock et al., 2012).

2.3.4 Risk factors for poor neurodevelopmental outcome

From a dynamic system theories approach, human development is influenced by genetic inheritance, nutrition, quality of care, SES, child rearing practices, disease processes and trauma. In addition to this, opportunity for play and refinement of skills, personality and motivation, level and quality of the stimulation and cognitive abilities all impact on developmental skill acquisition in a child (Aubert, 2015). Developmental outcome in children with CHD will be viewed within the framework of this approach. The cause of adverse neurodevelopmental outcome in children with CHD is multifactorial. Factors are often interrelated, and are also likely to be cumulative in nature (Wilson et al., 2015; Long et al., 2011; Robertson et al., 2011). In the light of the diversity of the risks for neurodevelopmental morbidity in the child with CHD, the child should be viewed holistically, considering multiple factors when risk is evaluated (Mussatto et al., 2014).

Current known patient and management-related risk factors only explain between 30 and 40% of the variance in neurodevelopmental outcome in children with CHD (Wilson et al., 2015; Gaynor et al., 2015; Mussatto et al., 2015; Martinez-Biarge et al., 2013). Many risk factors for adverse neurodevelopmental outcome are not modifiable, such as innate patient factors including genetic abnormalities, parental level of education and SES (Tabbutt et al., 2012). Only a few of the identified risk factors for poor neurodevelopmental outcome can potentially be modified in order to reduce the vulnerability of the CNS (Gaynor et al., 2015). These include delaying elective delivery to 39 weeks gestation and implementing CNS protection strategies during the pre-operative and post-operative periods (Tabbutt et al., 2012).

The most important risk factors for poor neurodevelopmental outcome will be presented below. They will be discussed under type and severity of CHD, children requiring cardiac surgery in early infancy, children with cyanotic types of CHD not requiring surgery in infancy, and peri-operative risks, patient-specific risks and sociodemographic risks.

2.3.4.1 Type and severity of the congenital heart disease

The severity of the CHD is associated with neurodevelopmental outcome. The more complex the CHD, the poorer the neurodevelopmental outcome has shown to be (Gaynor et al., 2015; Mussatto et al., 2015; Marino, 2013; Martinez-Biarge et al., 2013; Sananes et al., 2012; Tabbutt et al., 2012; Goldberg et al., 2011; Long et al., 2011; Hoskoppel et al., 2010; Simons et al., 2010).

Children with milder forms of CHD have shown to have a low incidence of developmental delay and DD (Rollins and Newburger, 2014; Marino et al., 2012); whereas more complex forms of CHD including moderate two-ventricle CHD (coarctation of the aorta, complex semilunar valve disease, VSD, VSD with comorbidities, TOF, TAPVD) are associated with increasing numbers of children presenting with developmental delay and DD (Marino et al., 2012). Severe two-ventricle or palliated single-ventricle CHD (TGA, truncus arteriosus, interrupted aortic arch, TOF, pulmonary atresia, tricuspid atresia and HLHS) is associated with a very high incidence of developmental delay and DD (Davidson et al., 2015; Marino et al., 2012; Tabbutt et al., 2012).

The need for multiple surgeries would be associated with more severe or complex forms of CHD; and is therefore also associated with worse neurodevelopmental outcomes (Mussatto et al., 2015; Tabbutt et al., 2012; Fuller et al., 2009).

2.3.4.2 Surgery in early infancy

Age at first cardiac surgery is associated with neurodevelopmental outcome (Majnemer et al., 2009). Children with more severe forms of CHD often require cardiac surgery in infancy (Marino et al., 2012; Tabbutt et al., 2012; Long et al., 2011; Snookes et al., 2010; Dittrich et al., 2003). Cardiac surgery itself poses a risk in early infancy. Cerebral perfusion and oxygenation may be compromised during cardiac surgery with CPB (Donofrio and Massaro, 2010). Inadequate cerebral perfusion and metabolism, temperature alterations, and cardiogenic emboli during cardiac surgery may result in hypoxic-ischaemic reperfusion injury. Complications can also arise post-operatively including cardiac arrest, infection and poor cerebral perfusion. These post-operative complications pose an additional risk for brain

injury (Majnemer et al., 2009) and may adversely affect neurodevelopmental (Marino et al., 2012; Long et al., 2011; Snookes et al., 2010; Dittrich et al., 2003).

Cardiac surgery with CPB during infancy is associated with impaired cognitive and motor development outcomes (Marino et al., 2012). Studies have shown these children to have more problems in reasoning, learning, executive function, inattention and impulsive behaviour, and language and social skills when compared to their healthy same-aged peers. Survivors of infant cardiac surgery were also found to be more likely than the general population to require remedial and EI therapy services including physiotherapy (PT), occupational therapy (OT) and speech therapy (ST) (Gaynor et al., 2015; Marino, 2013).

2.3.4.3 Cyanotic heart defects not requiring surgery in infancy

Children with cyanotic heart defects who do not require cardiac surgery in infancy may avoid some of the risks associated with open-heart surgery. However, these children are still to be considered at high-risk for developmental delays due to the effects of chronic hypoxemia caused by their underlying CHD. They may also be at risk later in childhood when they may need to undergo palliative or reparative surgeries (Marino et al., 2012).

Cyanotic infants with oxygen saturation (SpO_2) less than 85% have shown a higher incidence of neurological abnormalities (Owen et al., 2011; Donofrio and Massaro, 2010), and adverse neurodevelopmental outcomes have been reported in children with cyanosis beyond two years of age (Rappaport, 2015).

2.3.4.4 Peri-operative risk factors

Regulating the stress response and managing peri-operative factors can have an important impact on the neurodevelopmental outcome of infants who undergo cardiac surgery using CPB (Naguib et al., 2015).

2.3.4.4.1 Cardiopulmonary bypass

Nearly all surgery for complex CHD is performed on CPB with cross-clamping of the aorta (Tabbutt et al., 2012). During CPB, the infant brain may be subjected to global or focal ischaemia caused by gaseous or particulate micro emboli and hypo-perfusion (Dittrich et al., 2003). Cardiac surgery with CPB provokes a pronounced systemic inflammatory response (McCrindle et al., 2014; Tabbutt et al., 2012; Gessler et al., 2009). Brain dysfunction or encephalopathy is frequently accompanied by a general inflammatory response (Gessler et al., 2009). Longer CPB duration has been associated with worse neurodevelopmental outcome (Bellinger et al., 2011; Bellinger et al., 2003; Bellinger et al., 1999; Bellinger et al., 1995).

The concern for neurodevelopmental outcome relates to the longer exposure of the brain to CPB-induced pro-inflammatory cytokines (Sananes et al., 2012). Long-term neurodevelopmental sequelae associated with CPB include neurologic, developmental and behavioural deficits (Bellinger et al., 2011; Gessler et al., 2009; Bellinger et al., 2003; Bellinger et al., 1999; Bellinger et al., 1995).

2.3.4.4.2 Deep hypothermic circulatory arrest

Cardiothoracic surgeons may make use of DHCA due to the small structures of the heart and/ or the need for aortic arch reconstruction. DHCA is performed with deep hypothermia, and for periods during the surgery, there is no systemic blood flow (Tabbutt et al., 2012). The adverse impact of DHCA on neurodevelopmental outcome could possibly be attributed to hypoxic-ischaemic injury to the brain (Tabbutt et al., 2012; Bellinger et al., 2011). DHCA has also been associated with clinical seizures (Tabbutt et al., 2012).

Concerns have been voiced about longer durations of DHCA, with both Tabbutt et al. (2012) and Wypij et al. (2003) suggesting that a DHCA time exceeding 41 minutes to be of concern. However, Fuller et al. (2009) reported that DHCA for repair of single ventricle and biventricular CHD was however not predictive of worse neurodevelopmental performance at four years of age.

2.3.4.4.3 Aorta cross-clamp time

During the repair of intracardiac malformations the aorta is cross-clamped and the heart is arrested. Cross-clamping of the aorta results in a period of time in which there is no blood supply to the myocardium (Talwar et al., 2015; Schlensak, 2005). Once the cardiac surgery is completed the aortic cross-clamp is released and the heart is suddenly re-perfused with blood with a very high partial pressure of oxygen due to its exposure to the CPB circuit. As a result, the post-cardiac surgery myocardium is exposed to the dramatic extremes of ischaemia and reperfusion. Ischaemic reperfusion injury after cardiac surgery may manifest as arrhythmias, myocardial stunning, low cardiac output, and peri-operative myocardial infarction (Turer and Hill, 2010). The longer the cross-clamp time is, the greater the risk of myocardium suffering ischaemic-reperfusion damage when the aortic cross-clamp is released (Talwar et al., 2015; Turer and Hill, 2010; Schlensak, 2005).

To conclude the discussion on peri-operative risk factors, the landmark Boston circulatory arrest study (BCAS) has followed the neurodevelopmental outcome of the largest cohort of infants who underwent cardiac surgery between 1988 and 1992 longitudinally, providing invaluable insights on the effects of peri-operative strategies on developmental outcome. In their study, 177 infants were randomly assigned to deep hypothermia with either circulatory arrest or low-flow bypass support during surgical repair for TGA. Bellinger and colleagues have followed-up in excess of 80% of these children at one year of age (Bellinger et al., 1995), four years (Bellinger et al., 1999) eight years (Bellinger et al., 2003) and 16 years (Bellinger et al., 2011). They found that total circulatory arrest to support vital organs during cardiac surgery is associated with poorer developmental and behavioural outcomes. However, when reviewing outcomes of the BCAS one has to keep in mind that contemporary peri-operative strategies differ significantly from those used when the adolescents in the BCAS had heart surgery as infants nearly 20 years ago.

The BCAS and the desire to address modifiable surgical risk factors have resulted in advances in anaesthetic and surgical procedures aimed at protecting the brain (Tabbutt, 2013). With the exception of a higher haematocrit level during CPB, no other intraoperative interventions or procedural modifications have shown improvements in neurodevelopmental outcomes (Tabbutt, 2013). No significant differences were found on neuropsychological

testing or structural brain imaging between low-flow CPB and DHCA (Marino, 2013; Bellinger et al., 2011). Mussasto et al. (2015) also found no differences in cognitive, language, or motor outcomes for children that had CPB in comparison with those who did not undergo CPB.

Overall, risk factors related to cardiac surgery appear to play a limited role in the neurodevelopmental morbidity seen in CHD survivors (Gaynor et al., 2014; Von Rhein et al., 2012). This highlights the potential importance of patient-specific and sociodemographic factors, as well as abnormal brain development in determining neurodevelopmental outcome (Bellinger et al., 2011).

2.3.4.5 Medical complications and haemodynamic instability in the post-operative period

Haemodynamic instability and medical complications during the post-operative period may have an adverse effect on the brain during infancy. The developing brain has been shown to be vulnerable during the period of synaptogenesis and growth from the sixth month of gestation into the first year of life. Exposure to barbiturates, benzodiazepines and other neurotropic drugs during anaesthesia and ICU stay may result in widespread apoptotic neurodegeneration resulting in the death of millions of neurons. The excitotoxic consequences of ischaemic events are also amplified in the developing brain (Dittrich et al., 2003).

2.3.4.5.1 Cardiopulmonary resuscitation

Children with CHD may experience acute medical events, including cardiac arrest (Rollins and Newburger, 2014). Children who need cardiopulmonary resuscitation tend to experience a period of decreased cerebral perfusion and hypoxia. Depending on the duration of the cardiac arrest, limited or widespread injury may be caused to the brain structures that are most sensitive to oxygen and nutrient deprivation. This may result in permanent neurological injury, predisposing the child to subsequent neurological impairment and/or developmental delays and disorders (Rollins and Newburger, 2014; Marino et al., 2012; Sananes et al., 2012; Majnemer et al., 2009).

2.3.4.5.2 Prolonged hospital length of stay

Prolonged hospital length of stay may occur because of the severity of the CHD and/ or a complicated medical course (Marino et al., 2012; Majnemer et al., 2009). The need for pre-operative mechanical ventilation (Long et al., 2012b) and/ or prolonged hospital length of stay (Mussatto et al., 2015; Tabbutt, 2013; Sananes et al., 2012; Von Rhein et al., 2012) are associated with poorer developmental outcome. In addition, the need for repeated hospitalisation, as is often the case in more severe types of CHD, is also associated with worse developmental outcome (Long et al., 2011; Majnemer et al., 2009; Dittrich et al., 2003).

Hospitalisation results in periods of immobilisation, limited developmentally appropriate stimulation and decreased opportunities for play and practice of developmental skills that may negatively affect motor and cognitive development (Dittrich et al., 2003). Surgery and hospitalisation early in life requiring anaesthesia and the administration of analgesics may result in localised pain sensitivity (hyperalgesia) which may continue for years after the cardiac surgery, negatively affecting motor development (Long et al., 2011).

Marino et al. (2012) and Long et al. (2011) both reported that longer post-operative cardiac ICU length of stay and a hospital length of stay exceeding two weeks to be independently associated with poorer later cognitive function. Long et al. (2012b) found that increased hospital length of stay was also associated with poorer gross motor outcome in infancy.

2.3.4.5.3 Peri-operative seizures and stroke

Seizures are a common manifestation of acquired brain injury in children during the immediate post-operative period following cardiac surgery, and occur in approximately 30% of children with CHD (Gunn et al., 2012). Seizures may occur for no identifiable reason, but sometimes are secondary to an acute ischaemic or haemorrhagic event (Martinez-Biarge et al., 2013). Peri-operative seizures are associated with an increased risk of poorer neurodevelopmental outcome and neurological abnormalities (Davidson et al., 2015; Marino et al., 2012; Sananes et al., 2012; Sarajuuri et al., 2009).

Stroke is seen on MRI in 10 to 30% of infants with CHD, both before and after surgical repair. Strokes are often not clinically evident, but can cause later motor deficits and other neurodevelopmental problems (Martinez-Biarge et al., 2013; Sananes et al., 2012; Owen et al., 2011).

2.3.4.6 Patient-specific risk factors

The presence of the following comorbidities with CHD are associated with an increased risk of adverse neurodevelopmental outcome (Marino et al., 2012). Patient factors were found to be significant determinants of neurodevelopmental outcomes in children with CHD, as opposed to surgical management strategies (Fuller et al., 2009).

2.3.4.6.1 Prematurity and low birth weight

In addition to delayed maturation of the brain evident in some term newborns with CHD, some infants with CHD have the additional risk associated with being born prematurely. Infants with CHD born prematurely (gestational age of less than 37 weeks), and with a birth weight of less than 1500 grams are at increased risk for neurodevelopmental morbidity (Tabbutt, 2013; Chock et al., 2012; Long et al., 2012b; Marino et al., 2012; Sananes et al., 2012; Goff et al., 2011). Approximately 15% of neonates with CHD are born prematurely and/or with a low birth weight (Goff et al., 2011).

2.3.4.6.2 Genetic abnormalities associated with developmental disorders

Genetic disorders or syndromes occur in up to 30% of children with CHD (Martinez-Biarge et al., 2013; Marino et al., 2012). DS, Williams's syndrome, Noonan syndrome, CHARGE syndrome, VACTERL association, and deletion 22q11 are all genetic abnormalities associated with CHD (Marino et al., 2012). Neurodevelopmental outcome is strongly and independently associated with the presence of an underlying genetic abnormality (Martinez-Biarge et al., 2013; Marino et al., 2012; Long et al., 2011). Developmental outcome in children with CHD with DS is presented under section 2.3.6.

2.3.4.6.3 Neuroimaging abnormalities and microcephaly

There is a high prevalence of microcephaly in children with CHD. The prevalence of microcephaly is related to disease severity, and is reported in between 8 and 36% of children with CHD. The presence of microcephaly is associated with worse neurodevelopmental outcome (Marino et al., 2012; Goldberg et al., 2011; Long et al., 2011; Hoskoppel et al., 2010; Majnemer et al., 2009).

Neuroimaging literature is of the opinion that up to 59% of term infants with CHD experience some form of brain injury before undergoing cardiac surgery. Ischaemic lesions are observed in 21 to 41% of the population, with white matter injury occurring in 7 to 27%, PVL affects 17 to 38%, and strokes are evident in up to 30% of infants on neuroimaging studies (Owen et al., 2011). Neuroimaging abnormalities have shown to be associated with developmental delays and disorders in children with CHD (Marino et al., 2012).

2.3.4.6.4 Gender and ethnicity

Gaynor et al. (2015), Sananes et al. (2012) and Majnemer et al. (2012) all reported male gender to be associated with poorer developmental outcome, especially relating to cognitive and fine motor skills. Recent evidence suggests that there is a gender-specific response to hypoxic ischaemic injury to the immature CNS due to intrinsic differences in the male-female cell death pathways. Boys appear to be more vulnerable to a glutamate-mediated excitotoxicity cascade following hypoxic-ischaemic injury resulting in neuronal apoptosis (Majnemer et al., 2012).

Naguib et al. (2015) and Gaynor et al. (2015) noted that ethnicity potentially could be associated with poorer neurodevelopmental outcome, but currently this association has not been well established. Gaynor et al. (2015) reported that children of white ethnicity had poorer neurodevelopmental outcome. This finding however needs to be interpreted with caution against the background that the majority of participants in all neurodevelopmental outcome studies to date have been of white ethnicity (Gaynor et al., 2015).

2.3.4.6.5 Feeding problems and growth failure

Children with inadequate nutrition may tire easily, and be too weak and have inadequate energy for typical age-related play and exploration (Long et al., 2011; Dittrich et al., 2003). Poor growth and the need for tube feeding are associated with poorer developmental outcome (Mussatto et al., 2015). The relationship between growth and developmental outcome in children with congenital heart disease is presented under section 2.4.8.

2.3.4.6.6 Sociodemographic factors

There is growing evidence that non-modifiable patient-specific factors such as SES and level of parental education, as well as modifiable factors such as the home environment and parenting practices may be important determinants of later developmental functioning in children with CHD (Sarrechia et al., 2015; Sananes et al., 2012; Tabbutt et al., 2012). Lower levels of maternal education (Tabbutt et al., 2012; Majnemer et al., 2009) and lower SES is associated with worse developmental outcome in children with CHD (Gaynor et al., 2015; Mussatto et al., 2015; Naguib et al., 2015; Tabbutt et al., 2012; Majnemer et al., 2009), especially relating to cognitive ability (Sarrechia et al., 2015; Sananes et al., 2012; Von Rhein et al., 2011). Lower SES negatively impacts a family's ability to access both healthcare and EI services that potentially might have a positive influence on the child's developmental outcome (Riehle-Colarusso et al., 2015).

Typically, socioeconomic factors are not modifiable but supportive parenting practices can mediate the effect of poverty on brain development in children (Mussatto et al., 2015). Parenting practices, including maternal overprotection, are associated with poorer developmental outcome in children with CHD (Mussatto et al., 2015; Majnemer et al., 2009). Maternal overprotection may unnecessarily limit physical activity and social interaction of the child that can adversely affect their development (Sarrechia et al., 2015; Dittrich et al., 2003). Furthermore, parents' expectations of their child may also influence developmental outcome (Riehle-Colarusso et al., 2015).

2.3.5 Neurodevelopmental outcomes in children with congenital heart disease

2.3.5.1 Introduction

Neurodevelopmental difficulties occur in as many as 50% of CHD survivors (Mussatto et al., 2015; Knowles and Bull, 2012; Wernovsky, 2008). For many children and their families, the impact of the developmental difficulties on their daily lives is far more significant than that of the CHD itself (Wernovsky, 2008).

The spectrum of neurodevelopmental impairment is broad in children with CHD. Some children have minimal to no impairment, whilst others may be severely affected (Rollins and Newburger, 2014). Severe global developmental delay is relatively uncommon, but a characteristic pattern of mild or combined disabilities across multiple developmental domains has emerged (Mussatto et al., 2015). Injury to the white matter can result in cerebral palsy (Long et al., 2011). However, severe neurological deficits, such as cerebral palsy, epilepsy, hearing and visual impairment are uncommon and only affect around 5% of children with CHD (Martinez-Biarge et al., 2013; Knowles and Bull, 2012; Marino et al., 2012; Robertson et al., 2011; Hoskoppel et al., 2010).

Despite the heterogeneity in methodology between studies investigating neurodevelopmental outcome in children with CHD, results have shown a consistent pattern of developmental impairment (Martinez-Biarge et al., 2013; Sananes et al., 2012). These studies consistently revealed a pattern of mild motor and cognitive delays after cardiac surgery in early infancy (Tabbutt, 2013; Snookes et al., 2010). However, very few studies have described the neurodevelopmental status of neonates and infants with CHD before surgery (Limperopoulos et al., 2000).

Children with CHD experience neurodevelopmental problems through infancy, childhood and adolescence into adulthood (Brosig et al., 2014; Marino, 2013). By school entry, many children with CHD present with developmental delays across a number of developmental domains, including gross and fine motor, cognitive, and language deficits, behavioural problems, inattention and hyperactivity. These developmental deficits may be associated with greater difficulties in performing everyday activities and achieving independence in

personal maintenance tasks such as eating, dressing and toileting (Majnemer et al., 2009). Knowles and Bull (2012) reported that mild neurological problems might affect up to 25% of children with CHD. These authors reported that only 21% of children had completely normal mobility, cognition and self-care skills for their age, whilst 37% were moderately disabled.

There is considerable variability in neurodevelopmental outcome in adolescents following cardiac surgery in infancy (Bellinger et al., 2011). It has become evident that the developmental outcomes and needs of children with CHD change over time and with age (Mussatto et al., 2015; Mussatto et al., 2014). The societal costs of early childhood developmental delay are enormous and could have an impact across the lifespan. Developmental delay requires early developmental intervention services and special educational support. These costs will increase exponentially if the need for special education and developmental delays are not addressed effectively to optimise outcome. Adverse neurodevelopmental outcomes may also negatively impact on the child's later potential for education, lifetime employment and earnings (Mussatto et al., 2015).

2.3.5.2 Patterns of developmental delay and impairment

A better understanding is emerging of the patterns of neurodevelopment in children with CHD (Robertson et al., 2011). Children with CHD present with a distinctive pattern of neurodevelopmental and behavioural impairment characterised by mild impairments in cognition, motor skills, language, inattention, impulsivity, impaired executive function and psychosocial maladjustment (Gaynor et al., 2014; Mussatto et al., 2014; Marino, 2013; Martinez-Biarge et al., 2013; Knowles and Bull, 2012; Marino et al., 2012; Sananes et al., 2012; Robertson et al., 2011; Gerdes and Flynn, 2010; Matsuzaki et al., 2010). Moreover, there are often accompanying psychological issues such as anxiety, and depression (Marino, 2013).

Delays in cognitive, language and motor development are common in infancy (Brosig et al., 2014). Brosig Soto et al. (2011) found that nearly half of children were delayed in at least one developmental domain. However, early developmental outcomes have not been found to be highly predictive of school age developmental performance (Mussatto et al., 2015).

It is well established that children with more complex forms of CHD have more significant developmental delays (Sarrechia et al., 2015). The prevalence and severity of the developmental delay increase with disease severity and are associated with several genetic syndromes (Marino et al., 2012). Table 2.1 depicts the association between disease complexity and developmental disability.

Table 2.1 CHD complexity and the presence and severity of developmental disability

Severity of CHD	No disability	Mild disability	Severe disability
Mild	90%	8%	2%
Moderate	70%	20%	10%
Severe	40%	45%	15%
Palliated	30%	50%	20%
Syndromic	5%	65%	30%

(Adapted from Marino et al., 2012, p1147)

Patterns of developmental delay in each of the main domains of development will be discussed below.

2.3.5.2.1 Motor development

The majority of studies investigating motor outcomes in children after cardiac surgery have revealed some degree of persistent impairment in fine and/or gross motor function (Marino et al., 2012; Snookes et al., 2010). Motor deficits appear to be more significant than cognitive deficits in younger children with CHD (Wilson et al., 2015; Mussatto et al., 2014; Martinez-Biarge et al., 2013; Long et al., 2012b; Sananes et al., 2012; Tabbutt et al., 2012; Hoskoppel et al., 2010; Snookes et al., 2010; Fuller et al., 2009; Joynt et al., 2009). Gross motor delays are reported more frequently in infancy, whereas fine motor delays become more apparent by the age of two years (Sananes et al., 2012). Long et al. (2012a) concurred, reporting moderate motor delays in up to 10% of children with CHD aged two years.

Long et al. (2012b) investigated the gross motor development of 50 children with CHD who underwent cardiac surgery in infancy on the Alberta Infant Motor Scales (AIMS). They found that the children showed delays in gross motor development at four, eight, 12 and 16 months

of age, with 62% of the children exhibiting atypical gross motor development during the first year of life. Matsuzaki et al. (2010) investigated the neurodevelopmental outcome of one-year-old Japanese children with CHD following cardiac surgery on the Bayley Scales of Infant Development, Second Edition (BSID-II). They similarly reported that delays in gross motor development were common.

Limperopoulos et al. (2002) reported that up to 42% of children undergoing cardiac surgery with CPB exhibited delays in gross and/or fine motor skills at a mean age of 19 months on the Peabody Developmental Motor Scales (PDMD-4). When Majnemer et al. (2006a) re-evaluated the same cohort of children at five years of age, it was found that the motor delay persisted, with 49% exhibiting gross motor delays, and 39% had fine motor delays.

Gross and fine motor delay occurred more often in children undergoing palliative procedures, whereas fine motor delays were associated with DHCA time, microcephaly, and the number of hospitalisations (Marino et al., 2012). Motor performance was also poorer in children with cyanotic and complex lesions (Lata et al., 2015; Hövels-Gürich et al., 2006). Sarajuuri et al. (2009) found that gross motor development in children with single ventricle physiology was particularly delayed at the age of one year, and that children who had HLHS tended to show more globally delayed development. The aforementioned studies suggest that some degree of fine or gross motor impairment is common in survivors with complex CHD (Marino et al., 2012). Cardiac intervention may also be complicated by a stroke. More than half of the children who suffer a stroke in the peri-operative period experience ongoing sensory and/or motor impairments, with hemiplegia being the most common finding (Davidson et al., 2015; Rollins and Newburger, 2014).

Environmental factors have a significant impact on motor outcomes. Prolonged and repeated hospitalisation (Long et al., 2011; Dittrich et al., 2003), hyperalgesia (Long et al., 2011), musculoskeletal impairments (Long et al., 2011) and hypotonia (Rollins and Newburger, 2014) can all adversely affect gross motor and fine motor development. Maternal overprotection may further contributes to poor motor outcomes (Knowles and Bull, 2012). Delayed milestone acquisition in prone is common in children with CHD as a result of a lack of exposure to prone positioning. Prone positioning is often avoided due to respiratory compromise, immobilisation in hospital and post-sternotomy (Long et al., 2011).

Reduced endurance during physical activity is also associated with delayed motor development (Hövels-Gürich et al., 2006).

Fine and gross motor functioning is critical to overall physical functioning and depending on the severity of the motor impairments, may also affect cognitive, behavioural and psychosocial outcomes as well (Marino et al., 2012). Motor development outcomes may be variable over time due in part to the natural variability that occurs throughout typical infant gross motor development (Long et al., 2012b). At school age, 42.5% of children who underwent cardiac surgery in infancy still exhibit motor problems. The risk of having some degree of motor difficulty was shown to be six times greater, and the risk of severe motor impairment was eleven times greater for children with CHD compared to their healthy peers at school-going age (Marino et al., 2012).

Reports on motor outcomes in children with CHD in the literature are conflicting with some authors reporting that in some children early motor impairments tend to resolve over time (Wilson et al., 2015; Mussatto et al., 2014; Chock et al., 2012; Hoskoppel et al., 2010), whilst other authors report motor problems persisting throughout childhood and adolescence (Riehle-Colarusso et al., 2015; Schaefer et al., 2013; Von Rhein et al., 2012). The contradictory findings may possibly be explained by the varying patient profiles of the children included in these studies relating to both age and disease severity.

2.3.5.2.2 Cognitive development

Cognitive difficulties tend to become more apparent as the developmental skills become more complex with increasing age (Wilson et al., 2015; Mussatto et al., 2014; Martinez-Biarge et al., 2013; Long et al., 2012b; Tabbutt et al., 2012; Sananes et al., 2012; Snookes et al., 2010). Long et al. (2012a) noted mild cognitive delays in 17% and moderate cognitive delays in 2% of children aged two years with CHD. Cognitive deficits in children not requiring cardiac surgery in infancy are often subtle or absent (Tabbutt et al., 2012). There is an increased frequency of poor cognitive outcomes in children with more complex types of CHD, including TGA, TOF, single ventricle physiologies and HLHS (Riehle-Colarusso et al., 2015). Children who have neurological abnormalities and/ or abnormalities on neuroimaging studies were also shown to have worse cognitive outcomes (Von Rhein et al., 2011).

The patterns of developmental impairment in children with CHD displayed during the preschool years place them at high risk for difficulties as they go on to face the challenges and demands of the school environment (Sananes et al., 2012). Mild cognitive difficulties are cumulative and limit the child as they grow older and enter school (Sarrechia et al., 2015; Knowles and Bull, 2012). Despite their intelligence quotient (IQ) being in the normal range (Bellinger et al., 2011; Donofrio and Massaro, 2010), many school-aged children and adolescents with CHD display mild cognitive deficits.

One in three children with CHD have educational concerns raised by parents, the teacher, or the child (Davidson et al., 2015; Wilson et al., 2015; Martinez-Biarge et al., 2013). It is estimated that up to 50% of school-aged children with CHD require rehabilitation services (including PT, OT and ST) and remedial educational services (Gaynor et al., 2015; Riehle-Colarusso et al., 2015; Wilson et al., 2015; Knowles and Bull, 2012; Marino et al., 2012). According to Bellinger et al. (2011), 33% of school-aged children followed up as part of the BCAS required tutoring, 25% received special education and 17% had to be kept back at least one grade in school.

Mild cognitive deficits that are present in childhood may persist into adulthood (Riehle-Colarusso et al., 2015; Schaefer et al., 2013; Von Rhein et al., 2012), limiting educational achievement, employability and ultimately HRQOL (Davidson et al., 2015; Gaynor et al., 2015; Sarrechia et al., 2015; Wilson et al., 2015; Marino et al., 2012; Bellinger et al., 2011).

2.3.5.2.3 Language development

Children who have CHD with genetic syndromes or have undergone extracorporeal membrane oxygenation therapy (ECMO) are at a higher risk for sensorineural hearing loss. This hearing loss may be subtle and may go unidentified during the first year of life (Marino et al., 2012). Hearing loss may impair normal language development. Language difficulties tend to become more apparent as the skills become more complex with increasing age (Wilson et al., 2015; Mussatto et al., 2014; Martinez-Biarge et al., 2013). Language is one of the neurodevelopmental aspects most frequently affected in school-age children with CHD (Rollins and Newburger, 2014).

Mild speech and language delays reported after cardiac surgery in pre-school children with CHD; problems however seem less marked by school age. Subtle delays in expressive and receptive language have been reported in up to 40% of children with CHD (Knowles and Bull, 2012; Gerdes and Flynn, 2010).

In some children with CHD, language deficits relate to the level of cognitive functioning, while for other children it appears that language dysfunction may be an area of particular deficit in itself (Gerdes and Flynn, 2010). At school entry, language impairments may contribute to the social and academic challenges faced by children with CHD (Sarrechia et al., 2015; Brosig et al., 2014; Gerdes and Flynn, 2010).

2.3.5.2.4 Behavioural and psychosocial outcomes

There is growing consensus that children with CHD are at increased risk of behavioural difficulties and social incompetence (Davidson et al., 2015; Wilson et al., 2015; McCusker et al., 2013; Bellinger et al., 2009). The reported prevalence of psychosocial problems in children with CHD ranges between 15 and 25% (Brosig et al., 2014; Rollins and Newburger, 2014; Marino et al., 2012).

Children with CHD are three to four times more likely to present with inattention and hyperactivity than the population norm (Wilson et al., 2015; Tabbutt, 2013; Tabbutt et al., 2012). Up to 50% of children present with signs of inattention and hyperactivity (Mahle, 2015; Liamlahi et al., 2014; Marino et al., 2012). Cardiac surgery with CPB during infancy is thought to increase the risk of attention deficits (Davidson et al., 2015; Wilson et al., 2015; Gerdes and Flynn, 2010). Children with CHD with attention deficit hyperactivity disorder (ADHD) are at high risk of poor academic performance, and social and behavioural difficulties in childhood (Rollins and Newburger, 2014; McCusker et al., 2013; Schaefer et al., 2013; Marino et al., 2012). In addition, children with CHD have been found to be at a slightly increased risk for autism spectrum disorders compared with the population norm (Marino et al., 2012).

2.3.6 Developmental outcomes in children with congenital heart disease with Down syndrome

An important feature of children with DS is that their development is considerably delayed when compared to their typically developing peers (Van Gameren-Oosterom et al., 2011). Children with DS acquire gross motor and fine motor skills at a slower rate compared to typically developing children (Alsaied et al., 2016; Bertoti and Schreiner, 2015). Intellectual disability and hypotonia are present in nearly all children with DS (Visootsak et al., 2011).

Hypotonia and joint laxity contribute significantly to the delay in acquisition of gross motor skills. Children with DS also experience difficulties in postural and antigravity control, as well as balance and coordination (Bertoti and Schreiner, 2015; Visootsak et al., 2011). Motor impairments, may also result in secondary impairments related to cognition, communications and socialisation (Bertoti and Schreiner, 2015; Visootsak et al., 2011). Intellectual disability results in difficulties with academic activities such as reading, writing and mathematics (Alsaied et al., 2016; Van Gameren-Oosterom et al., 2011). School-aged children with DS show significant impairments in executive brain function (Alsaied et al., 2016). Impairments in both expressive and receptive language, and speech problems are prevalent in children with DS (Alsaied et al., 2016; Van Gameren-Oosterom et al., 2011; Visootsak et al., 2011). Other developmental disorders associated with DS include autism spectrum disorder (7%) and ADHD (6 to 9%) (Alsaied et al., 2016; Van Gameren-Oosterom et al., 2011).

As indicated above children with known genetic syndromes such as DS tend to have significant delays across all developmental domains (Mussatto et al., 2014). In addition, children with CHD are at increased risk for neurodevelopmental problems (Alsaied et al., 2016). The neurodevelopmental outcome after cardiac surgery is worse for children with genetic syndromes than for children without a genetic syndrome (Gaynor et al., 2015; Mussatto et al., 2015; Naguib et al., 2015; Marino et al., 2012; Tabbutt et al., 2012; Goldberg et al., 2011; Long et al., 2011; Fuller et al., 2009; Joynt et al., 2009). Worse outcomes in children with genetic abnormalities may be related to gene-environment interactions involving susceptible genes in multiple biological systems (including inflammatory and

oxidative pathways, coagulation cascades and the response to hypoxia/ischaemia) that may exacerbate the extent of the CNS injury after cardiac surgery (Marino et al., 2012).

The impact that CHD has on the neurodevelopment of children with DS is largely unknown (Alsaied et al., 2016). Most neurodevelopmental outcome studies in children with CHD conducted to date have specifically excluded children with chromosomal abnormalities, as chromosomal abnormalities associated with CHD are also independently associated with developmental delays and disorders (Rappaport, 2015). This has resulted in very little information being available on the course of development in children presenting with both CHD and DS, despite them being at even greater risk of adverse neurodevelopmental outcomes (Visootsak et al., 2011). Only studies by Alsaied et al. (2016) and Visootsak et al. (2011) have specifically investigated the impact of CHD on neurodevelopmental outcome in children with DS.

Alsaied et al. (2016) performed a single centre retrospective chart review of 1092 children younger than 18 years with DS that included 36 infants and toddlers with 12 children with DS with CHD and 24 with DS without CHD. Neurodevelopment in children younger than three years was determined using the BSID-III. They reported significant early motor and language delays in children younger than three years with DS with CHD. Visootsak et al. (2011) compared the developmental outcome of 12 children with AVSDs with DS and 17 children with DS without CHD using the BSID-III. They found that children with CHD with DS had significantly worse motor outcomes than children with CHD without DS. Cognitive and language development was poorer in children with CHD with DS compared to those with DS alone, but not significantly so. They attributed poorer developmental performance in children with CHD with DS to the fact that pre-operatively these children presented with poorer endurance and tired more easily. Post-operative hypotonia, asymmetry and decreased levels of alertness were also believed to contribute to worse developmental outcomes. CHD with DS requiring early surgical intervention and initial prolonged hospitalisation could also be seen to limit early therapeutic intervention which could also have negatively affected developmental outcome.

The combined results of the studies by Visootsak et al. (2011) and Alsaied et al. (2016) can be viewed to similarly suggest that children with CHD with DS have worse developmental

outcomes than children with CHD or DS alone across all developmental domains, in particular with regard to motor development.

Mussatto et al. (2014) conducted one of the only neurodevelopmental outcome studies to have included children with genetic abnormalities in the sample of a longitudinal neurodevelopmental follow-up study. Twenty percent of their study sample had genetic syndromes, including DS. They reported that genetic comorbidities were a risk factor for adverse neurodevelopmental outcome, and that 74% of the participants with known genetic syndromes in their study were found to have severe developmental delays. For children with genetic syndromes, cognitive and language scores on the BSID-III declined over time, and motor scores consistently remained poor.

2.3.7 Decreasing developmental morbidity in children with congenital heart disease: Implications for clinical practice

The AHA (2012) published a specific guideline targeting the identification and management of neurodevelopment in children with CHD (Marino et al., 2012). Consensus opinion is that developmental surveillance should form part of routine cardiac care (Marino et al., 2012), Periodic developmental surveillance, screening, evaluation, and re-evaluation at specific age points, including the first year of life, at school entry, middle school, and again in adolescence is recommended (Mahle, 2015; Mussatto et al., 2014; Marino, 2013; Marino et al., 2012). The goal of the guideline is to identify those children at greatest risk of developmental morbidity through childhood and adolescence, and to create opportunities for early developmental intervention and support to optimise the development, academic, behavioural, psychosocial, and adaptive functioning of the child (Knutson et al., 2016; Marino et al., 2012). Evaluation should also include growth monitoring, neuromotor examination, and hearing screening (Marino et al., 2012).

In accordance with the AHA (2012) guideline children with a genetic abnormality or syndrome are to be considered at high risk of developmental delay and disability. Both Alsaied et al. (2016) and Visootsak et al. (2011) recommend that in children with DS development be evaluated soon after birth, and they be referred for early developmental intervention (Alsaied et al., 2016; Visootsak et al., 2011).

Early developmental intervention in children with CHD is discussed in Chapter 7.

2.3.8 Childhood development in developing countries

A large number of children in developing countries are exposed to multiple risks for poor development. In addition to a diagnosis of CHD, other factors such as poverty, poor health and inadequate nutrition influence developmental outcome in children living in developing countries, including SA (Grantham-McGregor et al., 2007). Social disadvantage is considered a major risk to the childhood development. Poverty is associated with low levels of maternal education, increased maternal stress and depression, and inadequate developmental stimulation within the home. These are all factors that negatively affect childhood development (Grantham-McGregor et al., 2007). A lack of responsive parenting and inadequate stimulation within the home affects childhood development by disrupting the brain's neuronal circuitry (Engle et al., 2007). Appropriate interactions between a caregiver and child are critical to the development of the necessary cognitive and social-emotional skills that will serve as the foundation of later academic success (Engle et al., 2007).

As previously highlighted (Refer to 1.2) development outcomes for children living with CHD in developing countries are likely to be negatively impacted by late diagnosis (Reuters, South Africa, 2015), a lack of access to specialist care (Hoosen et al., 2010a; Hoosen et al., 2010b), the availability of mechanical circulatory support technologies (Carte Blanche, 2017; Hoosen et al., 2010a) and long waiting periods for cardiac surgery (Hoosen et al., 2010a; Hoosen et al., 2010b). Delayed treatment, prolonging the duration of cardiovascular compromise, could potentially increase the magnitude of the neurological insult suffered by children with CHD in developing countries.

Furthermore communicable diseases such as HIV may also threaten childhood development (Refer to 1.2). HIV-infection in infancy may cause severe encephalopathy resulting in severe developmental impairment. Even in HIV-infected children with less severe outcomes, there is an increased risk of developmental delay across all developmental domains (Potterton et al., 2010; Walker et al., 2007). The pathways from poverty to poor childhood development are shown in Figure 2.1.

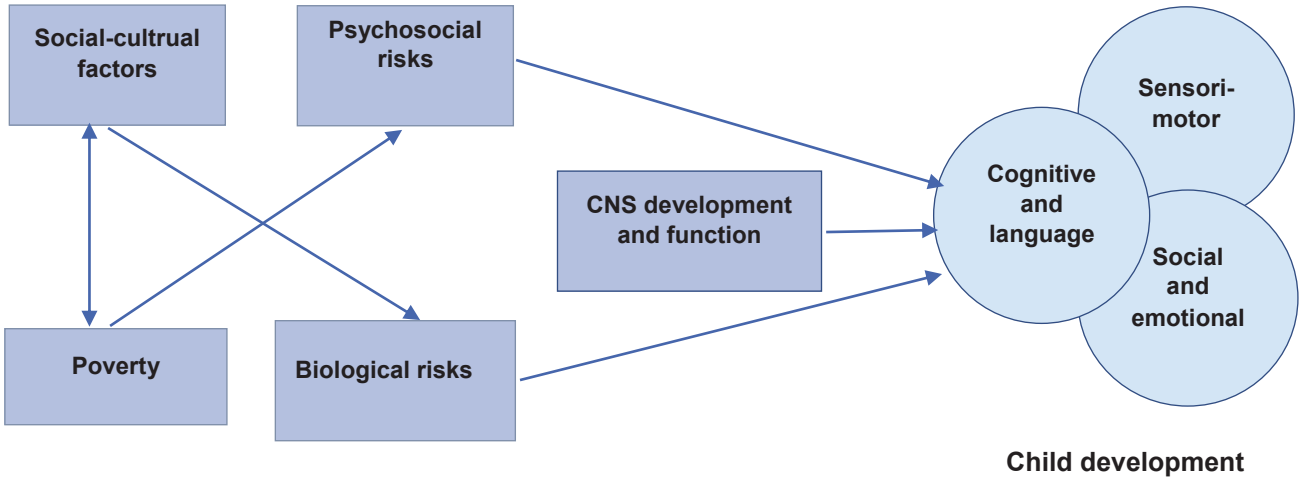

Figure 2.1 Pathways from poverty to poor development (Walker et al., 2007, p 146).

2.3.9 Summary

Children with CHD are at risk of neurodisability regardless of the severity of their cardiac disease. A better understanding has begun to emerge of the patterns of neurodevelopment in children with CHD, and the patient-specific and management- specific factors that place these children at increased risk of developmental morbidity. Children with CHD have been found to present with a distinctive pattern of neurodevelopmental and behavioural impairment characterised by mild impairments in cognition, motor skills, language, inattention, impulsivity, impaired executive function and psychosocial maladjustment. The extent and nature of the deficits have been found to change with developmental age.

Apart from CHD, children in developing countries are exposed to multiple other risks for poor development associated with social disadvantage, including inadequate stimulation within the home, and increased maternal stress and depression resulting in unresponsive parenting and inadequate nutrition. In addition, communicable diseases, especially HIV co-infection, may also threaten developmental outcome.

Based on neurodevelopmental outcome findings, the American Heart Association (2012) guidelines recommend regular neurodevelopmental follow-up should form part of routine

cardiac care. On diagnosis of developmental problems, child should be referred for EI services in order to optimise functional outcome and family participation. However, the model best suited to deliver EI services in this population in yet to be determined.

2.4 GROWTH FAILURE AND FEEDING DIFFICULTIES IN CHILDREN WITH CONGENITAL HEART DISEASE

2.4.1 Introduction

Inadequate nutrition is a coexisting concern for children with CHD. Nutritional deficiency, growth failure and feeding problems are associated with worse developmental outcome. Growth status is now considered an important measure of the child with CHD's health and wellbeing. (Irving, 2011). Therefore, it was deemed pertinent to review the role of nutrition in CHD outcomes.

2.4.2 Growth trends in children with congenital heart disease

Growth is considered an important global indicator of children's health and wellbeing (Okoromah et al., 2011). Nutritional status during the early years of life has a significant impact on the overall health and wellbeing of the child (Grantham-McGregor et al., 2007; Martorell, 1999). Improved survival in children with CHD has brought to light the fact that children with CHD face several challenges relating to both growth and feeding, which in turn affect development (Daymont et al., 2013; Ravishankar et al., 2013; Roman, 2011; Knirsch et al., 2010). Children with CHD may present with growth failure, as well as a feeding dysfunction (Medoff-Cooper et al., 2016).

Growth failure is a risk factor for adverse developmental outcome in children with CHD, and is associated with impaired cognitive and motor development outcomes (Lata et al., 2015; Irving, 2011). Nutrition is however considered a modifiable risk factor for developmental outcome (Medoff-Cooper et al., 2016; Knirsch et al., 2010). As a result, there is an increased interest in nutrition-related aspects, such as feeding ability and growth trajectories, in this population as possible predictors of developmental outcome (Medoff-Cooper et al., 2016).

2.4.3 Malnutrition and growth failure in children with congenital heart disease

Malnutrition (undernutrition) and growth failure are common in children with CHD, both before and after medical and surgical intervention (Irving, 2011; Varan et al., 1999). The

severity of the malnutrition can range from mild to severe, resulting in failure to thrive (FTT) (Wheat, 2002; Varan et al., 1999). In more severe cases, malnutrition may result in permanent physical or developmental impairment (Wheat, 2002). There is also a high occurrence of protein energy malnutrition (PEM) in children with CHD (Knirsch et al., 2010). Growth failure, FTT, growth retardation, undernutrition and PEM are terms that are used interchangeably to describe less-than-adequate weight gain and poor physical development in young children (Cole and Lanham, 2011; Irving, 2011). Malnutrition results from a diet that provides inadequate calories and protein for growth, or where the child is unable to fully utilise the food he/she consumes due to illness (Blössner and De Onis, 2005).

The WHO (2006) criteria for the determination of malnutrition indicates that a cut-off z-score of ≤−2 standard deviations (SD) below the age- and gender-specific median for the normal population classifies as a low weight-for-age z-score (WAZ) (underweight), low height-for-age z-score (HAZ) (stunting), and low weight-for-height z-score (WHZ) (wasting). Z-scores of ≤−2 SD equate to moderate malnutrition, stunting and wasting. Z-scores of ≤−3 SD below the age- and gender-specific median for the normal population equates to severe malnutrition, stunting and wasting. Weight-for-age z-scores between −2 and 2 indicate normal nutrition (Wang and Chen, 2012; Roman, 2011; WHO, 2006). Stunting (height-for-age ≤ -2 SD below the normal) is to be considered an indicator of chronic malnutrition (Ravishankar et al., 2013; Wang and Chen, 2012).

Even if the child with CHD is born with a weight that is appropriate for gestational age, growth failure typically becomes apparent during the neonatal period if haemodynamically significant CHD is present. Estimates of malnutrition in unrepaired CHD in infants ranges between 50 and 90% (Roman, 2011). Infants and young children are the most vulnerable to malnutrition and FTT because of their high nutritional requirements for growth and development (Blössner and De Onis, 2005).

Malnutrition and growth failure can have a notable effect on the outcome of cardiac surgery (Okoromah et al., 2011; Varan et al., 1999). Post-surgery growth, and in particular weight gain, is considered a measure of surgical success and disease management (Irving, 2011).

In addition, children with poor growth tend to be more susceptible to infectious diseases, such as meningitis and pneumonia, which also contribute to mortality and morbidity (Okoromah et al., 2011).

2.4.4 Causes of growth failure in children with congenital heart disease

The causes of malnutrition and FTT in children with CHD is most often multifactorial. Causes can be divided into three key categories namely; inadequate intake of nutrients, increased energy needs and ineffective nutrient absorption (Roman, 2011).

2.4.4.1 Inadequate calorie intake

Inadequate calorie intake has been shown to be the most important cause of growth disturbances in children with CHD (Lata et al., 2015; Daymont et al., 2013; Wheat, 2002; Varan et al., 1999). Reasons for inadequate calorie intake may include fatigue during feeding and malabsorption (Daymont et al., 2013; Wheat, 2002). Chronic hypoxia causes both dyspnoea and tachypnoea during feeding resulting in the child tiring easily, reducing the quantity of food consumed (Wheat, 2002). Cardiopulmonary dysfunction may therefore lead to an inability to feed adequately, children may require a longer time to feed, or may present with a lack of appetite and refuse food intake (Da Rosa Pereira et al., 2015; Roman, 2011). Feeding problems may also contribute to inadequate food intake (Refer to section 2.4.7) (Daymont et al., 2013; Roman, 2011; Wheat, 2002).

2.4.4.2 Increased metabolism

Increased metabolism due to the cardiac defect causes a state of constant metabolic stress, resulting in increased energy expenditure (Lata et al., 2015; Daymont et al., 2013; Knirsch et al., 2010; Wheat, 2002; Varan et al., 1999). Children with CHD also have less body fat and a higher percentage of lean body mass, which increases their metabolic rate (Roman, 2011; Long et al., 2011; Wheat, 2002). Other reasons for increased energy expenditure include tachypnoea, tachycardia, cardiac hypertrophy, polycythaemia, increased sympathetic nervous system activity, and sepsis (Roman, 2011).

2.4.4.3 Inadequate and ineffective nutrient absorption

Inadequate or ineffective nutrient absorption after birth in children with CHD may occur due to vomiting, reduced splanchnic blood flow, poor gastric emptying and altered gut motility, oedema of the small intestine (in the case of right-sided cardiac failure), excessive nutrient loss including protein and trace nutrients, gut mucosal atrophy leading to malabsorption in children with significant pre-existing malnutrition, and IGF-1 deficiency (Roman, 2011).

2.4.4.4 Additional factors contributing to growth failure

Other factors that may play a role in growth failure in children with CHD include abnormal foetal blood flow and intrauterine growth restriction (Knirsch et al., 2010) and low birth weight (Roman, 2011; Knirsch et al., 2010).

The extent and type of malnutrition may be related to characteristics of the CHD, including presence of cyanosis, CCF or PHTN (Daymont et al., 2013; Tabbutt et al., 2012; Roman, 2011). The duration of cyanosis appears to be more important than the severity of the CHD in determining the extent of the malnutrition (Daymont et al., 2013; Tabbutt et al., 2012; Roman, 2011). According to Okoromah et al. (2011) most children with CHD showed wasting rather than underweight and stunting. Wasting was associated with acyanotic CHD, whilst stunting was linked to cyanotic CHD. Children with complex CHD show large, early, and sustained decreases in growth trajectories (Daymont et al., 2013).

Chromosomal abnormalities (Daymont et al., 2013; Knirsch et al., 2010) and non-cardiac abnormalities (Daymont et al., 2013) are linked to poor growth. (Refer to 2.4.6). Cardio active medication is also known to have nutrition-related side effects (Roman, 2011). Malnutrition may also be due to decreased growth factors and hormonal changes (Lata et al., 2015; Daymont et al., 2013).

Figure 2.2 proves a schematic representation of the factors affecting growth in children with CHD.

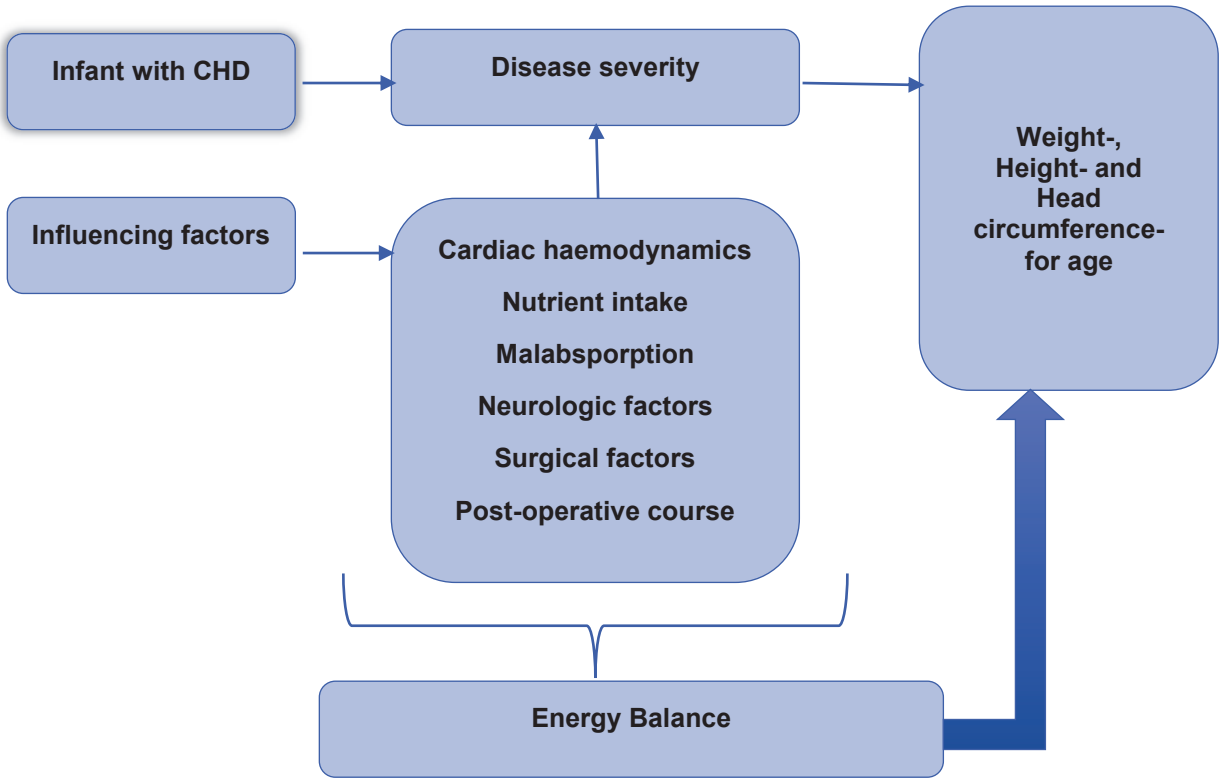

Figure 2.2 Potential influences on growth in children with CHD (Irving, 2011, p 29).

2.4.5 Growth outcomes in children with congenital heart disease

The consequences of malnutrition in the short term for children with CHD include an impaired ability to fight infection and for surgical wounds to heal optimally. Infants with poor nutritional status tend to have a prolonged ICU and total hospital length of stay post-cardiac surgery (Roman, 2011). Over the longer term, malnutrition results in suboptimal growth and impaired physical development (Roman, 2011). Growth status in childhood is also linked to adult height and weight (Daymont et al., 2013; Tabbutt et al., 2012). Some children with CHD do show significant growth catch-up after corrective or palliative cardiac surgery. Children who undergo surgery in infancy have a better chance of improving both their weight and length growth (Roman, 2011).

There are a limited number of published studies reporting specifically on the growth outcomes of young children with CHD. Studies in developed countries include those by

Medoff-Cooper et al. (2016), Costello et al. (2015), Daymont et al. (2013), Ravishankar et al. (2013) and Irving (2011).

Medoff-Cooper et al. (2016) investigated the association between growth and device-assisted feeding and the early neurodevelopmental outcome in infants with CHD. Their prospective cohort study included 72 infants with complex CHD who underwent cardiac surgery. They found that 30% of their study participants had weight for age z-scores of ≤ -2 SDs from the norm. Infants with complex CHD who required device assisted feeding and those who showed growth failure at three months of age were found to be at risk of developmental delay at six and 12 months of age.

Costello et al. (2015) aimed to determine the prevalence of growth failure in infants and young children with CHD and establish the relationship between poor growth, feeding difficulties, disease severity, and nutritional intervention on outcomes. This prospective cohort study in Australia collected growth data for 78 children with CHD younger than three years. They found that 23% of their participants demonstrated growth restrictions as evidenced by *z*-scores of ≤−2 for weight-for-age and 21% for length-for-age. Growth failure was found to be high especially prior to cardiac intervention. No relationship was found in their study between the presence of cyanosis and growth. Half of the participants were found to have feeding difficulty on admission, and this was associated with poorer growth.

Daymont et al. (2013) described the growth outcomes of 248 young children with CHD in a retrospective cohort matched study in the US. They found that children with single ventricle physiology and those requiring surgical intervention showed a significant decrease in weight-for-age and length-for-age, which appeared within the first month of life, then peaked near four months of age, and persisted through 24 to 36 months of life. By 36 months, it was found their growth had not yet caught up. They also noted microcephaly in 3% of children with CHD, making them more likely to have microcephaly than their healthy same aged peers. They deducted that the presence of microcephaly was indicative of restricted brain growth during the critical developmental period of infancy, which potentially could have lifelong consequences for neurodevelopment.

Ravishankar et al. (2013) conducted a multi-centre randomised controlled clinical drug trial in North America to investigate whether Enalapril improved growth and ventricular function in 230 children with single ventricle physiology. They concluded that poor height-for-age z-score trajectories in early infancy were associated with neurodevelopmental disability.

Irving (2011) looked at patterns of weight change in infants with CHD following neonatal cardiac surgery, aiming to identify potential predictors of growth failure. She reported that 50% of infants with CHD in their study exhibited poor growth early on in life and 30% fell below the third percentile for weight on standard growth charts for age and gender during infancy. They reported a pattern of poor growth in the birth to three-month interval across gender.

Published data on the growth outcomes of children with CHD in developing countries, and in particular African countries, is scant. Studies published in developing countries include those by Lata et al. (2015), Okoromah et al. (2011), Vaidyanathan et al. (2008) and Varan et al. (1999).

Lata et al. (2015) investigated the neurodevelopmental outcome of 75 children aged six to 30 months in India. As part of their outcomes they assessed growth, and reported that 57.3% of the children in their study had weight ≤ -3 SD from the norm. Low pre-operative weight and older age at surgery were found to be associated with post-operative weight below the tenth percentile.

Okoromah et al. (2011), in an observational case-control study done in Nigeria, investigated the prevalence of malnutrition in 73 children with CHD aged three to 192 months. They reported a prevalence of malnutrition of 90.4% in the children in their study, and in 61.2 % of cases the malnutrition was found to be severe.

Vaidyanathan et al. (2008) conducted a prospective cohort study in India, investigating the determinants of malnutrition in 476 children with CHD under the age of five years. They reported a very high prevalence of malnutrition in children undergoing cardiac surgery. At three-month post-cardiac surgery they found that 55.9% had weight-for-age, and 26.3% had height-for-age ≤ -2 SD from the norm, while 27.7% had weight-for-age and 10.1% had

height-for-age ≤ -3 SD from the norm.

Varan et al. (1999) investigated the prevalence of malnutrition and growth failure in 89 Turkish children with CHD aged one to 45 months. They reported that 65.2% of the children were below the fifth percentile for weight, and 41.6% were below the fifth percentile for both weight and height. Moderate to severe malnutrition was more common in children with cyanotic CHD.

2.4.6 Growth outcomes in children with congenital heart disease and Down syndrome

Children with DS have different growth trajectories from the general paediatric population. Children with DS have been shown to have lower birth weights and a slower growth rate. They are also characterised by short stature and a tendency to overweight and obesity in later childhood (Zemel et al., 2015; Bravo-Valenzuela et al., 2011; Myrelid et al., 2002). Growth outcomes for children with DS have improved over recent decades due to advances in- and increased access to medical care (Zemel et al., 2015). Growth failure in infants with DS may occur due to feeding difficulties and other medical problems (Charleton et al., 2010).

There are few studies that have specifically investigated the growth outcomes in children with CHD with DS. Bravo-Valenzuela et al. (2011) retrospectively investigated the impact of CHD with DS, on the weight and height recovery after surgical correction in 181 children with DS, from birth until 18 years. They found that children with DS who had cardiac disease requiring surgical intervention showed greater weight and height impairments, with 55% of the children in their sample being malnourished and 60% stunted. Weight and height recovery after surgery occurred in most cases in a period of six months to one year.

Van Gameren-Oosterom et al. (2012), on the other hand, investigated growth outcomes in 890 Dutch children with DS. Of their sample 234 children were also diagnosed with CHD. They found that the growth outcomes of healthy children with DS and those with mild CHD to be similar. However, the children with severe CHD showed significantly poorer growth outcomes. These authors reported that growth failure arose in the first year of life, but no further growth deflection neither catch-up growth occurred.

Knirsch et al. (2010) examined the determinants of growth failure and their association with neurodevelopmental outcome in a sample of 107 infants in Switzerland, which also included infants with genetic comorbidity. Fifteen of the children in their sample had CHD with DS. They reported that the extent of the growth failure was significantly greater in children with CHD with genetic comorbidity, finding genetic comorbidity to be the single most significant predictor of poor catch-up growth post-surgery.

From the reported studies to date, it can be best concluded that children with mild CHD follow similar growth trajectories to healthy children with DS without CHD. Children with severe CHD tend to exhibit significant growth failure across all growth parameters. Infants tend to show considerable catch-up growth after corrective cardiac surgery in infancy.

2.4.7 Feeding problems in children with congenital heart disease

Feeding difficulties are common in children with CHD, with feeding dysfunction noted in upwards of half of children with CHD (Medoff-Cooper et al., 2016; Costello et al., 2015; Da Rosa Peirera et al., 2015; Brosig et al., 2014). Early sucking and swallowing difficulties have been associated with growth failure and poorer catch-up growth (Medoff-Cooper et al., 2016). Children undergoing cardiac surgery in infancy have a high risk of presenting with feeding difficulties up until the age of two years (Da Rosa Peirera et al., 2015). Feeding difficulties may present as swallowing dysfunction or gastroesophageal reflux disease (GORD) (Da Rosa Pereira et al., 2015).

Poor oral feeding post-cardiac surgery, and the need for a medical feeding appliance are associated with prolonged hospital length-of-stay and impaired HRQOL (Costello et al., 2015; Da Rosa Pereira et al., 2015; Tabbutt et al., 2012). The use of a feeding appliance may adversely affect cognitive development as it may interfere with the exploratory activities of a child (Da Rosa Pereira et al., 2015). Abnormal brain development (Mussatto et al., 2014), and brain immaturity resulting from the CHD (Medoff-Cooper et al., 2016) may result in abnormal feeding, and are considered to put the child with CHD at risk of developmental delay (Mussatto et al., 2014).

In addition, feeding problems may be exacerbated in children with CHD with genetic abnormalities or syndromes where feeding difficulties also arise for reasons unrelated to the CHD (Roman, 2011). Children with DS have feeding difficulties because of their poor oral motor function resulting from hypotonia of the oral musculature and a protuberant tongue which interferes with feeding (Charleton et al., 2010).

2.4.8 Relationship between growth and developmental outcome in children with congenital heart disease

Malnutrition and growth failure is a risk factor for poor developmental outcome in vulnerable children with CHD (Lata et al., 2015; Daymont et al., 2013; Tabbutt et al., 2012; Irving, 2011). The impact of poor growth on neurodevelopmental outcome in infants with CHD has not been widely studied to date (Ravishankar et al., 2013). Poor nutrition during the foetal period results in a reduction in brain size. The late foetal period is a period of rapid brain growth, and during this period the brain is particularly vulnerable to inadequate nutrition (Medoff-Cooper et al., 2016). Available literature suggests that adequate nutrition is essential to optimise brain growth during the first months of life (Medoff-Cooper et al., 2016).

Adequate nutrient intake in infancy is crucial to promote a positive energy balance to support brain growth, neurodevelopment, and physical maturation (Irving, 2011). Children who post-cardiac surgery still have unresolved cardiac problems, or those with genetic and other congenital abnormalities that affect growth may miss the critical window for appropriate growth (Roman, 2011). These children may have fewer body cells including adipose, muscle, and bone cells resulting in poor growth and delayed maturation of the bony skeleton, but also result in poor of motor skills. Children younger than three years with cyanotic heart defects younger, tend to have lower than normal intelligence scores, due to lower brain weight impairing cognitive function (Roman, 2011). The use of a medical feeding appliance, such as feeding tube, has also been found to be associated with an increased risk of poor cognitive and motor development outcomes (Medoff-Cooper et al., 2016).

Poor nutrition during the intrauterine period and early years adversely affects motor development and cognitive development (IQ scores are lower) in children with CHD, and results in deficient social skills, behavioural problems, decreased attention, learning

problems and poorer academic achievement at school (Medoff-Cooper et al., 2016; Lata et al., 2015; Irving, 2012; Okoromah et al., 2011; Martorell, 1999).

In addition, infants with CHD who have inadequate nutrition may lack the muscle strength and energy needed for typical age–related developmental activities. This would result in them tiring easily with physical activity resulting in delays in the achievement of age appropriate gross motor milestones (Long et al., 2011). Irving (2011) also found infants with growth failure to be more irritable and more difficult to parent.

2.4.9 Growth in children in developing countries

Growth in infants and young children is directly related to the socioeconomic environment in which they live (Lunn, 2002). Malnutrition and SES are closely linked in that poverty results in inadequate food being available for consumption (Grantham-McGregor et al., 2007; Martorell, 1999). In turn, inadequate nutrition due to poor socioeconomic circumstances has been found to inhibit brain growth (Balter, 2015).

Poverty-related factors including households' low socio-economic status, food insecurity, poor quality diets, poor maternal health before, during and after pregnancy, and the high prevalence of infectious diseases mediate growth failure in children living in developing countries (Grantham-McGregor et al., 2007; Lunn, 2002).

Children from developing countries grow more slowly (Lunn, 2002). Growth faltering in children in developing countries begins in utero or shortly after birth, becoming pronounced in the first 12 to 18 months of life. It is possible that it can even continue to around 40 months of age, after which it levels off. Some catch-up may occur but most stunted children remain stunted through to adulthood (Grantham-McGregor et al., 2007; Lunn, 2002). Sub-Saharan Africa and South Asia are home to three-quarters of the world's stunted children. In sub-Saharan Africa, 40% of children under the age of five years are stunted (Said-Mohamed et al., 2015; UNICEF-WHO-WB, 2015; UNICEF, 2013). Children from developing countries who are stunted have been shown to have poorer cognition, scholastic achievement, and psychosocial functioning in later childhood (Ravishankar et al., 2013; Grantham-McGregor et al., 2007). Growth failure during infancy has been implicated in impaired development of

executive function and poor school performance (Ravishankar et al., 2013; Okoromah et al., 2011; Grantham-McGregor et al., 1999; Martorell, 1999).

The poor socioeconomic circumstances of many families living in developing countries, is likely to amplify the growth-related challenges faced by children living there with CHD due the inability of parents to provide an adequate cardiac diet. This situation is even direr for single parent, female-headed households, where poverty and vulnerability to financial crisis and malnutrition is heightened (Amakali and Small, 2013).

2.4.10 Reducing growth failure in children with congenital heart disease: Implications for clinical practice

It is important to identify the cause of poor growth in children with CHD in order to improve growth outcomes (Daymont et al., 2013). Monitoring of growth trajectories and feeding skills should be implemented in at risk children with CHD (Medoff-Cooper et al., 2016; Da Rosa Peirera et al., 2015; Roman, 2011). Where indicated nutritional interventions such as dietary supplementation and nutritional counselling could be beneficial in limiting growth failure (Irving, 2011). Strategies to improve feeding skills, such as speech and feeding therapy should be recommended for children requiring device assisted feeding (Mussatto et al., 2014; Wheat, 2002).

2.4.11 Summary

Growth failure is common in children with CHD due to inadequate caloric intake, increased metabolic demand and nutrient malabsorption. Many children with CHD also experience feeding difficulties including swallowing dysfunction and GORD, which contributes to growth failure. Malnutrition and growth failure place children with CHD at risk of poorer developmental outcome. Growth outcomes of children with DS and CHD are similar to children with DS alone, but is dependent on disease severity. Considerable catch–up growth does take place after cardiac intervention. Regular monitoring of growth and feeding skills is advised in children with CHD. Where indicated, nutritional interventions and feeding therapy could be beneficial in limiting growth failure in these children.

2.5 HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH CONGENITAL HEART DISEASE

2.5.1 Introduction

Improved survival and advances in the treatment of CHD allows for what is to be considered as an almost normal life for many children living with CHD (Amedro et al., 2015; Bertoletti et al., 2015; Werner et al., 2014; Eagleson et al., 2013; Nousi and Christou, 2010). However, survival is not necessarily synonymous with a good quality of life (Nousi and Christou, 2010). It is well documented that children living with CHD present with physical, neurodevelopmental and psychosocial morbidities related to complications of their cardiac disease and the treatment thereof. This may in turn have a significant impact on their wellbeing (Marino et al., 2016; Marino et al., 2010; Nousi and Christou, 2010).

Determining the health status and neurodevelopment of children with CHD has recently become a healthcare priority, but determining these outcomes alone will fail to paint the full picture of the true impact of CHD and its treatment on the child (Landolt et al., 2008). To better understand the full and ongoing extent of the impact of cardiac disease and its treatments on the lives of children, attention has to be focused on how CHD affects HRQOL through the various stages of childhood development, into adolescence and later adulthood (Amedro et al., 2015; Bertoletti et al., 2015; Knowles et al., 2014; Eagleson et al., 2013; Uzark et al., 2013; Nousi and Christou, 2010). Psychosocial difficulties of survivors, and poor coping and adaptation exhibited by families have become the new hidden morbidities of this high-risk population (Uzark et al., 2013; Majnemer et al., 2006b).

As HRQOL continues to emerge as an important outcome measure and health indicator (Pike et al., 2007), both healthcare professionals and parents have a responsibility to promote coping and the successful adaptation of the child with CHD in their daily environment and in their communities to ensure a good QOL (Mussatto, 2006).

2.5.2 Defining quality of life, health-related quality of life and wellbeing

There is a lack of consensus in the literature regarding the definition of, and conceptualisation of, quality of life (QOL) and health-related quality of life (HRQOL). QOL and HRQOL are separate, yet interrelated concepts (Eagleson et al., 2013; Pike et al., 2007).

QOL is defined as the perception of the individual of their wellbeing and general satisfaction with life (Majnemer et al., 2006b). QOL is dynamic and is affected by a person's ability to adapt to disparities in expected and experienced wellbeing, as well as the ability to maintain a level of functioning that allows for the pursuit of life goals (Pike et al., 2007).

HRQOL differs from QOL in that it characterises life when a medical condition and the treatment thereof is relevant. HRQOL reflects the perception of a person's health status as defined by the impact of a medical condition and its treatment on their life (Marino et al., 2010; Pike et al., 2007). HRQOL is a multidimensional construct, composed of the person's perception of the impact of disease and treatment on their functioning and ability to derive satisfaction in a variety of aspects of life, including in physical, psychological and social domains (Eagleson et al., 2013; Pike et al., 2007). Health and wellbeing are concepts closely related to HRQOL. The World Health Organisation (WHO) defines health as "a state of complete physical, mental, and social wellbeing and not merely the absence of disease or infirmity" (WHO, 1948). Wellbeing on the other hand, refers to the positive aspects of a person's life, such as positive emotions and life satisfaction (United States Department of Health and Human Services, 2014).

HRQOL can then be defined as the subjective impact of a specific illness and its treatment on the ability of the person to both function in and derive personal satisfaction from various physical, psychological, and social life aspects of health (Marino et al., 2016; Werner et al., 2014; Marino et al., 2010). A better understanding by healthcare professionals of parental perceptions of their child with CHD's HRQOL has the potential to improve both treatment and health outcomes (Marino et al., 2016).

Figure 2.3 provides a schematic representation of the relationship between cardiac disease-related morbidity and HRQOL.

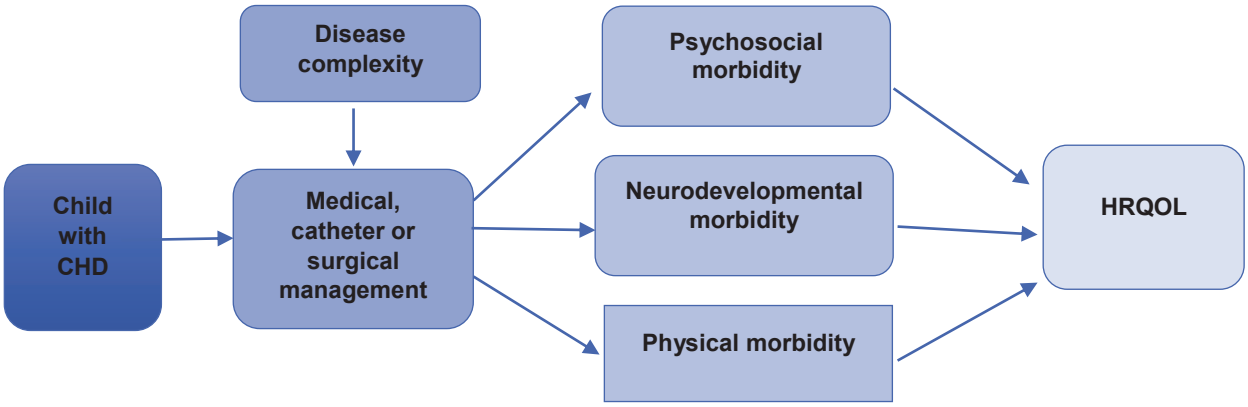

Figure 2.3 Relationship between cardiac disease-related morbidity and HRQOL (Marino et al., 2016, p12).

2.5.3 Factors affecting health-related quality of life in children with congenital heart disease

Children with CHD, especially those with more complex cardiac disease, are at risk of poorer long-term outcomes compared to their healthy same-aged peers. The psychosocial outcome of these children is shaped by the medical care they received in infancy, which may include recurrent hospitalisations and repeat procedures that may negatively affect parent-child attachment. More importantly though, these outcomes are influenced by how parents and the extended family integrate medical care and education with the psychosocial needs of the child (Berkes et al., 2010).

Numerous factors have been identified to have a negative impact on HRQOL in children with CHD. Factors influencing HRQOL may vary in accordance with the child's developmental age and level of physical growth (Marino et al., 2010; Nousi and Christou, 2010). The factors affecting HRQOL outcomes are however still poorly understood and little is known about determinants of HRQOL in this population (Pike et al., 2007).

Delayed physical growth with respect to height and weight is the single factor shown to be most significantly associated with poor HRQOL in children with CHD. The extent of the growth failure varies in accordance with the type and severity of the CHD (Nousi and Christou, 2010).

Parents and/or the child's physical health may impose restrictions on the child's level of physical activity (Nousi and Christou, 2010). Physical activity limitations also curb activities of daily living (ADL) such as walking, running and climbing stairs. Physical activity limitations in turn may also result in restrictions' in participatory activities such as play and social interactions with same-aged peers, negatively affecting socialisation and community participation, diminishing HRQOL (Amedro et al., 2015; Eagleson et al., 2013; Birks et al., 2006). Miatton et al. (2007) contradicted the aforementioned finding, noting that the physical activity levels of children with CHD were similar to that of their healthy same-aged peers. The conflicting reports can possibly be explained by the differing patient profiles in the represented studies with regard to disease severity. Physical activity is most often only limited in children with severe CHD, while most children with mild or moderate forms of CHD face very few limitations in this regard.

Anxiety and depression can result from frequent follow-ups and repeated hospitalisations, multiple medical procedures and the use of daily medications. Depression and anxiety often goes unrecognised or is overlooked in children with CHD as a result of the magnitude of other complications and concerns (Bertoletti et al., 2015; Nousi and Christou, 2010; Miatton et al., 2007). Children who undergo open heart surgery may also develop a poor body image due to the large scar on their chest (Nousi and Christou, 2010).

The family environment is an important determinant of HRQOL. Family functioning has an important impact on the life experiences and happiness of the child (Majnemer et al., 2006b). Parents who overprotect and project their own distress onto their child may not allow the child to take own initiative, leading to poor self-esteem and impaired HRQOL (Nousi and Christou, 2010). Contextual factors such as peers, family, school and the community also have an important impact on HRQOL in the child with CHD (Bertoletti et al., 2015).

Social disadvantage affects HRQOL outcomes in children with CHD. Low levels of parental education, prior to the diagnosis, may result in them not seeking or delay seeking of medical assistance, potentially worsening the child's health and outcome. Parents with low levels of education also tend to have difficulties in recognising their child's need for support, or they may ignore its importance, and consequently, their child may show symptoms of anxiety, depression or have behavioural problems (Nousi and Christou, 2010). Low SES of the family is associated with poor QOL of both the child with CHD and the family. Having to care for a child with CHD heightens the financial burden placed on the family, and financial difficulties may result in family and marital conflict (Nousi and Christou, 2010). Financial difficulties lead to increased levels of parental stress. High levels of parental stress is associated with poorer psychosocial wellbeing of the child with CHD (Dulfer et al., 2015; Majnemer et al., 2006b). Behavioural difficulties of the child are strongly associated with higher levels of parental distress (Miatton et al., 2007; Majnemer et al., 2006b). In turn, parents with increased distress are more likely to report on behavioural problems in their children (Spijkerboer et al., 2010).

Parental QOL may also influence the QOL of the child. The overlap of parental QOL and children's QOL is seemingly due to a shared family environment influencing wellbeing and functioning (Goldbeck and Melches, 2005). In addition, the ability of the child and family to cope and adapt to adverse experiences related to the child's CHD has a significant impact on the child's HRQOL (Bertoletti et al., 2015).

2.5.4 Establishing health-related quality of life in children with congenital heart disease

HRQOL measures allow for the determination of the impact of health on QOL. They can also be used to establish the burden of a chronic illness (CDC, 2016a). Establishing HRQOL in children with CHD is complicated by widely variable age, developmental stage and diagnoses (Garcia Guerra et al., 2014). Historically, HRQOL outcomes in CHD populations have been based on clinical assessment findings, and have had a motor development or functional focus (Eagleson et al., 2013; Berkes et al., 2010; Birks et al., 2006). Assessing HRQOL comprehensively requires not only looking at physical functioning and symptoms, but also at psychosocial and cognitive functioning (Varni et al., 1999).

There are several generic HRQOL measures, but disease-specific HRQOL measures for CHD are now becoming available (Bertoletti et al., 2015). In contrast to generic measures, disease-specific measures focus on the dimensions of health that are likely to be affected by a specific medical condition and its treatment (Berkes et al., 2010; Pike et al., 2007; Raat et al., 2006). HRQOL measures should be multidimensional and include physical, social, psychological, mental and functional aspects (Amedro et al., 2015).

Both child and parent reported experiences and outcomes are considered to be important in ascertaining the HRQOL of children with CHD over the longer-term. It is therefore recommended that multiple reporters be used to determine the HRQOL of children with CHD; including parent and child self-reporting, where the child is old enough (Knowles et al., 2014; Goldbeck and Melches, 2005). Furthermore, HRQOL needs to be assessed holistically, taking into account community, socioeconomic conditions, and the personal and interpersonal needs of the child to function and develop (Bertoletti et al., 2015). It is important to acknowledge that children do not have the capacity to alter their environment, as adults do. Their environment is determined for the most part by their parents (Bertoletti et al., 2015).

HRQOL in children with CHD needs to be assessed in infancy and toddlerhood, as this is the time during which most cardiac interventions take place. In younger survivors, parents or primary caregivers have to report on their perception of the child's HRQOL, as the child is too young and does not have the cognitive or language skills to provide a self-report (Werner et al., 2014). In most cases, it is mothers who report on HRQOL outcomes as they in most instances fulfil the role of primary caregiver (Berkes et al., 2010).

It is believed that parents provide a valid appraisal of their child's HRQOL (Eagleson et al., 2013; Majnemer et al., 2006b). Parent proxy reporting of their child's HRQOL in the case of children with CHD has however been shown to be variable, with some parents overestimating and others underestimating their child's health and performance abilities (Pike et al., 2007). Bertoletti et al. (2015), Knowles et al. (2014), Schaefer et al. (2013) and Tahirović et al. (2010) noted that parents perceived their child's HRQOL as poorer than the child did. Uzark et al. (2008), on the other hand, found that for the most part parents perceive their children's overall HRQOL to be comparable to that of their healthy same-aged peers.

The contradictory findings can potentially be explained by the varying participant profiles of the aforementioned studies with regard to disease severity (Uzark et al., 2008). Parental responses are also likely to be influenced by their stress levels (Spijkerboer et al., 2010), their hopes and expectations for their child, and how well they as a family are coping (Majnemer et al., 2006b). Family functioning has an important influence on parents' perception of life experiences and the happiness of their child (Majnemer et al., 2006b).

A child's perception of the impact of their disease on their life may differ from that of their parents, educators and healthcare professionals (Knowles et al., 2014). The divergent perceptions between parents and their children, so-called cross-informant variance, have been frequently and widely reported in the literature. This reflects the different but complementary perspectives that are both to be considered as equally important. The value of using multiple reporters in determining the HRQOL of the child with CHD is again highlighted (Amedro et al., 2015; Eagleson et al., 2013; Latal et al., 2009). Assessing the perceptions of both the parent and child, where age appropriate, are believed to provide a more comprehensive picture of the HRQOL of the child (Nousi and Christou, 2010).

Clinicians tend to rely solely on proxy reporting by parents and their own perceptions of the child's HRQOL (Goldbeck and Melches, 2005). Marino et al. (2009) goes on to highlight that important differences also exist in the HRQOL perceptions of parents and healthcare professionals. This further strengthens opinion that multiple reporters on HRQOL, including the child, parents and healthcare professionals are most likely to provide the most comprehensive view of the overall HRQOL outcome of the child.

2.5.5 Health-related quality of life outcomes in children with congenital heart disease

There has been increasing interest in studying HRQOL in children with CHD (Landolt et al., 2008). Whilst HRQOL has been investigated in the adult population for over a decade, the study of HRQOL in children and adolescents is a relatively new focus area (Bertoletti et al., 2015; Uzark et al., 2013).

HRQOL is not currently assessed as part of routine cardiac care (Amedro et al., 2015; Uzark et al., 2013), and there is limited published data on the psychosocial and HRQOL outcomes

of infants and young children living with CHD (Berkes et al., 2010; Miatton et al., 2007; Pike et al., 2007). To date the study by Werner et al. (2014) is the only study that has investigated HRQOL in children as young as one year. Studies by Eagleson et al. (2013), Berkes et al. (2010), Tahirović et al (2010) and Uzark et al. (2008) included children of wide ranging of ages, also including children as young as two years.

Studies done on the HRQOL outcomes in children with CHD are limited by several factors. These include small sample size, use of varied measurement tools, varied and wide ranging ages of participants, reliance on parent proxy-reporting of HRQOL and health status of the child and observed functional status, and often only a single dimension of HRQOL was the focus (Amedro et al., 2015; Werner et al., 2014; Marino et al., 2010).

HRQOL outcomes in children with CHD remain controversial, with findings throughout published literature being inconsistent and contradictory (Werner et al., 2014; Landolt et al., 2008). Some studies report HRQOL outcomes that are comparable to those of healthy same-aged peers, whilst others report impaired HRQOL (Amedro et al., 2015; Garcia Guerra et al., 2014; Werner et al., 2014; Eagleson et al., 2013; Pike et al., 2007; Mussatto, 2006). These contradictory findings highlight the challenges faced in establishing HRQOL in a growing child (Amedro et al., 2015).

HRQOL findings in children with CHD are conflicting when compared to norms for healthy and chronic illness populations (Eagleson et al., 2013). Mellion et al. (2014) found that both children and adolescents with mild and complex CHD had significantly lower HRQOL than their healthy same-aged peers, but similar HRQOL as children with other chronic paediatric diseases including diabetes, obesity and asthma.

Several factors have been reported to influence HRQOL outcomes. The impact of cardiac disease severity and the presence of cyanosis on HRQOL outcomes remain unclear (Eagleson et al., 2013). Congenital heart defects associated with cyanosis were found to be predictive of the physical wellbeing of the child (Schaefer et al., 2013). In contrast, Hövels-Gürich et al. (2007) found that HRQOL in children with cyanotic lesions was similar to that of children with acyanotic lesions, and comparable to that of their healthy same-aged peers.

A reason for the contradictory findings could be that the disease severity profiles of the samples may have differed.

Findings regarding the impact of disease severity on HRQOL outcomes are contradictory. Eagleson et al. (2013), Tahirović et al. (2010) and Uzark et al. (2008), on the one hand, found that the severity of the defect was related to HRQOL outcomes. Children with complex defects were found to have worse HRQOL outcomes. Complex CHD resulting in haemodynamic instability, cyanosis and CCF negatively affected functioning during ADL, and negatively influenced HRQOL (Birks et al., 2006; Tahirović et al., 2010). Macran et al. (2006), in turn, found that disease severity influenced HRQOL only in younger children with complex CHD. In contradictory findings, Amedro et al. (2015), Bertoletti et al. (2015), Latal et al. (2009) and Majnemer et al. (2006b) determined that the severity of the CHD was not significantly related to HRQOL outcomes.

The contradictory findings in the literature show disease severity not to be a reliable predictor of the longer-term psychosocial outcomes of the child with CHD. Rather, as Mussatto (2006) suggests, parents' perception of the impact of the cardiac disease, irrespective of the disease severity, play a more significant role in determining parents' view of their child's physical and psychosocial functioning. It was also established in various studies that around 20% of children with CHD have impaired psychosocial functioning, irrespective of disease severity (Knowles et al., 2014; Eagleson et al., 2013; Uzark et al., 2013; Berkes et al., 2010). Amedro et al. (2015), Uzark et al. (2013), Marino et al. (2009) and Pike et al. (2007) all found physical and psychosocial impairments had a significant impact on HRQOL. Furthermore, vision and hearing impairments (Knowles et al., 2014), as well as feeding difficulties were associated with poorer HRQOL (Werner et al., 2014).

Studies on associations between HRQOL and a range of variables, such as demographic factors, SES and surgical factors, have also produced inconsistent findings (Eagleson et al., (2013). Majnemer et al. (2006b) reported that surgical factors were not strong indicators of HRQOL outcomes. To the contrary, Schaefer et al. (2013), Latal et al. (2009) and Hövels-Gürich et al. (2007) reported a connection between the duration of CPB and DHCA and HRQOL outcomes relating to psychosocial wellbeing and autonomy. Older age at the time

of the first cardiac surgery and the need for multiple surgeries were also associated with worse HRQOL outcomes (Latal et al., 2009).

Eagleson et al. (2013) reported an association between age and HRQOL. HRQOL outcomes are believed to improve with age, with adolescents having a HRQOL comparable to their healthy same-aged peers (Latal et al., 2009). No connection was however found between gender and HRQOL (Latal et al., 2009). Children with CHD are particularly affected in terms of their physical and cognitive functioning in early childhood; and these children face the greatest risk for poor HRQOL outcomes. Appropriate interventions (including parent training regarding appropriate developmental stimulation, feeding assistance, and social and emotional interaction with their child), and the facilitation of adequate adaptation to the child's CHD may also serve to explain why over time children may be experience HRQOL similar to that of their healthy same-aged peers (Latal et al., 2009; Pike et al., 2007).

Higher SES has been found to be associated with better HRQOL outcomes in children with CHD (Amedro et al., 2015, Latal et al., 2009). Parenting style, levels of parenting stress, and family coping and adaptation to the child's cardiac disease also influenced the child's HRQOL (Knowles et al., 2014).

Cardiac interventions, regular use of medication, and non-cardiac comorbidities were independently associated with reduced HRQOL. The burden of cardiac intervention is considered to be cumulative over time (Knowles et al., 2014).

Most of the HRQOL research data collected to date has been in North America and Europe. The generalisability of these findings to all children with CHD is difficult due to cultural, socioeconomic and social diversity (Pike et al., 2007). In addition, most HRQOL studies that were conducted represent only a single CHD diagnosis, making the outcomes difficult to generalise to the general CHD population (Knowles et al., 2014).

Overall, the HRQOL of children with CHD would seem to be comparable to that of their healthy same-aged peers (Schaefer et al., 2013). Despite feeling that there were areas of their lives that could be improved upon, it appears that children develop successful

strategies for coping with any problems that their cardiac condition causes, even more so where the cardiac condition is corrected early in life (Marino et al., 2009; Birks et al., 2006).

2.5.6 Health-related quality of life outcomes in children with congenital heart disease and Down syndrome

Scant information is available on the HRQOL outcomes of children with CHD with DS who have undergone cardiac intervention. For the most part, children with chromosomal abnormalities have been excluded from outcome studies as the presence of a chromosomal abnormality was considered a confounding factor that independently influenced health-related outcomes (Garcia Guerra et al., 2014). Three studies were identified to have assessed HRQOL of children with genetic abnormalities including DS. It must be noted however, that Werner et al.'s (2014) study was the only study to investigate HRQOL in children with CHD with genetic abnormalities younger than four years.

Werner et al. (2014) determined the perceived HRQOL of 144 Austrian children, including those with genetic comorbidity, who had undergone cardiac surgery before the age of six months, using the Netherlands Organisation for Applied Scientific Research Academic Medical Centre Preschool Children Quality of Life (TAPQOL). They found that children with CHD with a genetic abnormality were at increased risk for reduced HRQOL due to the cognitive and neurodevelopmental impairments associated with genetic abnormalities.

Other studies to take note of are those by Garcia Guerra et al. (2014) and Van Gameren-Oosterom et al. (2011). Garcia Guerra et al. (2014) investigated the perceived HRQOL of 16 Canadian children aged four years with CHD who also had chromosomal abnormalities (including DS), who underwent cardiac surgery for complex CHD in infancy, using the Paediatric Quality of Life Inventory (PedsQL^{TM}). They similarly reported significantly worse HRQOL outcomes for children with CHD with genetic comorbidity when compared to their healthy same-aged peers, and when compared to children with CHD without genetic abnormalities. The children in their study with CHD with genetic abnormalities showed significantly lower scores across all HRQOL dimensions including emotional, social and physical functioning.

Van Gameren-Oosterom et al. (2011) investigated the QOL of a sample of eight-year-old Dutch children with DS using the TNO-AZL Children's Quality of Life (TACQOL). Similar to Garcia Guerra et al. (2014), they found that children in their study with DS had poorer HRQOL related to gross motor skills, autonomy and social and cognitive functioning in comparison with the normative sample.

Based on the available literature it can be concluded that children with CHD with DS are at increased risk of impaired HRQOL compared to children with CHD without DS, and compared to their healthy same-aged peers. Impaired HRQOL in young children with CHD with DS is associated with the cognitive and neurodevelopmental impairments that are characteristic of children with DS.

2.5.7 Improving health-related quality of life outcomes in children with congenital heart disease: Implications for clinical practice

Long-term HRQOL outcomes are important markers of the success of cardiac intervention aimed at maximising health and minimise symptoms, disability, and dysfunction. No cardiac programme is to be considered complete without attention being paid to the physical, psychological and social-emotional wellbeing of the child (Marino et al., 2010; Baker, 2008). Routine and ongoing screening of HRQOL is recommended as part of standard cardiac care (Eagleson et al., 2013). Subjective HRQOL information in combination with objective clinical assessment provides a comprehensive picture of physical, emotional and social concerns in the child with CHD (Pike et al., 2007).

HRQOL information empowers the cardiac team to counsel parents on the expected performance of their child in everyday life (Bertoletti et al., 2015; Garcia Guerra et al., 2014). It also prompts referral for intervention (Uzark et al., 2013), which may include developmental therapy, psychological and social support services (Majnemer et al., 2006b; Mussatto, 2006), and educational interventions to promote resiliency and coping (Eagleson et al., 2013; Mussatto, 2006). Intervention serves to optimise HRQOL in children identified as being at risk (Bertoletti et al., 2015; Werner et al., 2014; Eagleson et al., 2013; Uzark et al., 2013; Marino et al., 2010; Majnemer et al., 2006b). Specific tailored interventions need

to be developed to improve HRQOL outcomes in children with CHD in the future (Landolt et al., 2008; Pike et al., 2007).

2.5.8 Summary

The physical, neurodevelopmental and psychosocial morbidities related to cardiac disease and the treatment thereof may have a significant impact on the health and wellbeing of children living with CHD. In an attempt to better understand the full and ongoing extent of the impact of CHD on the lives of children, HRQOL has emerged as an important outcome measure and health indicator.

HRQOL refers to the perceived impact of the cardiac disease and its treatment on the function and ability of the child to derive satisfaction in a variety of aspects of life, including the physical, psychological and social domains. HRQOL in young children is established by parent-proxy reporting, which serves as a valid appraisal of their perception of their child's health and wellbeing. Parent proxy-reporting can be supplemented by the healthcare practitioner reporting.

Child-related and family-related factors impact on HRQOL in children with CHD. Child-related factors include treatment-related factors, impaired growth, physical activity limitation, physical symptoms related to the cardiac disease, social isolation and the presence of a genetic abnormality such as DS. Family-related factors include parental educational attainment, SES and parenting stress.

Routine and ongoing screening of HRQOL is recommended as part of standard care. Subjective HRQOL information used in combination with objective clinical assessment information provide a comprehensive picture of the physical, emotional and social concerns of the child. Where indicated, children should be referred for appropriate intervention to optimise HRQOL outcomes.

2.6 PARENTING STRESS AND THE BURDEN OF CARING FOR A CHILD WITH CONGENITAL HEART DISEASE

2.6.1 Introduction

Improved survival rates have seen CHD become the second most prevalent chronic illness in childhood (Bruce et al., 2014; Grønning Dale et al., 2013; Hartman and Medoff-Cooper, 2012). More parents than ever before are having to care for children living with CHD. The experience of raising a child with CHD has proven to be a challenge for many families (Brosig et al., 2007; Mussatto, 2006). The news that their child has a congenital heart defect suddenly and unexpectedly disrupts parents' expectations of a healthy infant and their world is forever changed. Parents must cope with both transitioning into parenthood and the diagnosis of CHD, with all its associated medical, financial, social, and emotional implications (Fonseca et al., 2012; Yildiz et al., 2009).

Parenting stress is defined as the psychological distress experienced by parents in trying to meet the demands of their parenting role Golfenshtein et al. (2016). Burden of care on the other hand refers to discomfort experienced by a parent in their caregiving role, which affects their health, psychosocial wellbeing, financial status and social life (Zarit et al., 1980).

Little is known about how parents' wellbeing is affected by having to care for a child with CHD (Grønning Dale et al., 2013). There is growing interest in the impact of a child's CHD on parents' psychological health, family life and parenting experiences, considering parents have a considerable influence on their child's health and development (Wei et al., 2016; Hearps et al., 2014; Grønning Dale et al., 2013; Rempel et al., 2013). Furthermore, there is a strong relationship between parental wellbeing and a child's health outcomes, further driving interest in this area (Moola, 2012).

The ongoing treatment of CHD; which may include the use of medication, regular follow-up and multiple interventions (Bruce et al., 2014; Vrijmoet-Wiersma et al., 2009), as well as comorbidities affecting neurodevelopment and HRQOL (Vrijmoet-Wiersma et al., 2009; Majnemer et al., 2006b), contribute to parenting stress.

Many parents are able to cope and successfully adapt to having a child with CHD (Bruce et al., 2014; Tak and McCubbin, 2002). However, for other parents the chronic health problems faced by their child due to their CHD place them at high-risk of experiencing ongoing stress (Bruce et al., 2014; Solberg et al., 2011; Vrijmoet-Wiersma et al., 2009). Ongoing stress affects a parent's ability to cope, undermines their health and wellbeing, as well their family functioning (Majnemer et al., 2006b). Over time, ongoing stress may manifest in psychological problems including anxiety and depression (Bruce et al., 2014; Solberg et al., 2011; Vrijmoet-Wiersma et al., 2009). Parents of children with CHD often feel hopeless and lack confidence and conviction in their parenting abilities (Connor et al., 2010; Vrijmoet-Wiersma et al., 2009; Brosig et al., 2007).

2.6.2 Stressors associated with psychosocial morbidity in parents of children with congenital heart disease

It has been established that parents of children with CHD experience higher levels of stress compared to parents of healthy children or parents of children with other chronic illnesses (Wei et al., 2016; Hearps et al., 2014; Grønning Dale et al., 2013; Harvey et al., 2013). Parents of children with CHD face a multitude of stressors that are unique to parenting a child with cardiac disease. These stressors affect their levels of stress and their sense of personal wellbeing (Soulvie et al., 2012; Lan et al., 2007).

Findings on the levels of stress experienced by parents of children with CHD in the literature are conflicting (Wei et al., 2016; Grønning Dale et al., 2013; Fonseca et al., 2012). Parental emotions change over time, based on their child's condition and the specific stressors in play at the time (Wei et al., 2016; Grønning Dale et al., 2013). This may in part explain the inconsistencies in the literature regarding the extent and impact of various parental stressors (Wei et al., 2016).

For the purpose of this literature review, the most important parental stressors will be discussed below.

2.6.2.1 Diagnosis, hospitalisation and cardiac surgery

Parents face a “roller coaster” of emotions when their child is diagnosed with a congenital heart defect. All parents face similar emotions irrespective of the severity of the cardiac disease (Wei et al., 2016). The emotions experienced range from shock, disbelief, fear, sadness, anxiety, and guilt to grief (Wei et al., 2016; Bruce et al., 2014; Hearps et al., 2014; Hartman and Medoff-Cooper, 2012). Parents feel the diagnosis comes at a considerable personal emotional cost (Connor et al., 2010). They feel ill-equipped to deal with their child’s heart condition (Hartman and Medoff-Cooper, 2012), and struggle to make decisions regarding the child’s care (Soulvie et al., 2012; Lan et al., 2007). Hospitalisation of the child, cardiac surgery, family separation and financial pressures exacerbate the emotional distress felt by parents during this time (Hearps et al., 2014).

Parents report experiencing extremely high levels of stress before their children go in for cardiac surgery (Wei et al., 2016; Harvey et al., 2013; Landolt et al., 2011; Solberg et al., 2011; Franck et al., 2010). Parents also report feeling extremely anxious whilst waiting for their children to come out of surgery (Wei et al., 2016). However, the most stressful and overwhelming experience for almost all parents of children undergoing cardiac surgery was seeing their child in the ICU after the surgery (Wei et al., 2016; Harvey et al., 2013; Franck et al., 2010). Multiple surgical interventions also increase parents’ vulnerability for ongoing psychological stress (Vrijmoet-Wierma et al., 2009). Hospitalisation in general was found to be moderately to very stressful for parents, regardless of the child’s cardiac disease severity (Harvey et al., 2013; Franck et al., 2010).

In addition, parents are concerned about their child’s future health and wellbeing (HRQOL), worrying about the prognosis and their child’s outcome over time. Parents have often voiced a sense of hopelessness and distress related to the aforementioned (Bruce et al., 2014; Connor et al., 2010).

2.6.2.2 Role stress and burden of care

Each parent has a unique reaction to stress and will exhibit varying degrees of anxiety (Bruce et al., 2014). Parents of a child with CHD often experience role strain (Lan et al., 2007). It is reported that mothers are more strongly affected by a child's cardiac disease than fathers (Yildiz et al., 2009). Mothers have been found to experience more stress than fathers based on their role within the family (Franck et al., 2010; Uzark and Jones, 2003; Goldberg et al., 1990). In addition, mothers of children with CHD experience an increased burden of care. This is by virtue of the fact that they tend to fulfil the role of primary caregiver, spending more time on and being actively engaged in the care of the child (Fonseca et al., 2012; Yildiz et al., 2009).

Parenting a child with CHD is considered to be more demanding and more time consuming (Bruce et al., 2014; Grønning Dale et al., 2013; Yildiz et al., 2009; Lawoko and Soares, 2006). This ongoing burden of care often results in increased levels of stress (Torowicz et al., 2010; Lawako and Soares, 2006), physical exhaustion and social isolation (Bruce et al., 2014; Grønning Dale et al., 2013; Yildiz et al., 2009). In addition to caring for the child with CHD, mothers are also responsible for domestic chores and caring for siblings (Harvey et al., 2013; Lawoko and Soares, 2002). A father's role is two-fold, caring for both the mother and child in the situation (Wei et al., 2016). In most cases, fathers are less involved in the care of the children as they fulfil the role of the primary breadwinner, responsible for providing the financial means of the family (Menahem et al., 2008). Single parent and female-headed households have been found to experience extremely high levels of stress associated with parenting a child with CHD as the burden of care is not shared with anybody (Amakali and Small, 2013; DeMaso et al., 1991).

2.6.2.3 Feeding difficulties and growth failure

Feeding plays an important role in the parent-child relationship (Bevilacqua et al., 2015). Feeding difficulties and growth failure are common in children with CHD, and serve as ongoing stressors for parents (Harvey et al., 2013; Soulvie et al., 2012; Hartman and Medoff-Cooper, 2012).

2.6.2.4 Severity of the congenital heart disease

It has been suggested that disease severity is not a reliable predictor of the longer-term psychosocial outcome of parents (Grønning Dale et al., 2013). Rather, parents perception of the impact of their child's CHD on the family, has proven to be a far more powerful predictor of parental stress, than the disease severity itself (DeMaso et al., 1991). It is acknowledged that levels of parenting stress may change over time in accordance with the developmental stage of the child and course of the illness (Goldberg et al., 1990).

Research findings on the relationship between disease severity and psychosocial problems in parents of children with CHD are divergent (Lawoko and Soares, 2006). Grønning Dale et al. (2013), Connor et al. (2010), Torowicz et al. (2010), Majnemer et al. (2006b) and Mörelius et al. (2002) all reported that the severity of the child's cardiac disease affected the levels of stress experienced by parents. Parenting a child with severe CHD was found to be more stressful than parenting a child with moderate or mild disease. The reasons for increased levels of stress in the case of parenting a child with severe CHD may be attributed to multiple stressors, including repeated cardiac surgeries, recurrent hospitalisations; as well as feeding problems, behavioural problems, and developmental delays and disorders in the child (Grønning Dale et al., 2013).

To the contrary, Hartman and Medoff-Cooper (2012) reported that parents of children with CHD experienced heightened levels of emotional distress irrespective of disease severity. The authors viewed disease severity to be less important than other factors such as sociodemographic stressors, coping strategies, and the excessive burden of care (Lawoko and Soares, 2006). Srichantaranit et al. (2010) found in addition to the aforementioned religion and cultural beliefs affected parents' experiences and wellbeing.

2.6.2.5 Age and characteristics of the child

Parenting stress in children with CHD has been shown to be especially high during infancy and toddlerhood. A heightened level of caregiving is required at this age, in addition to the stressors caused by the child's CHD. High levels of parenting stress have also been found to continue in the preschool years (Soulvie et al., 2012; Lee et al., 2007). Uzark and Jones

(2003), by contrast, found that the older the age of the child the higher the levels of parenting stress.

Other factors that influence the parent-child relationship are the parents' mental health, ability to cope and family functioning. The diagnosis of CHD can have a profound impact on the parent-child relationship (Doherty et al., 2009). Parents often feel stressed or defensive about their child, particularly if their child exhibits behavioural problems (Majnemer et al., 2006b).

Parents also report that children with CHD, especially those with severe disease, are often difficult to parent. Increased levels of stress are often related to the characteristics of the child, which make them difficult to parent (Soulvie et al., 2012; Uzark and Jones, 2003). Parents' view children with severe CHD as having difficult temperaments, characterised by being difficult to soothe and being irritable and moody. Irritable infants have been linked to maternal feelings of stress, inadequacy, fatigue and resentment (Torowicz et al., 2010). The exact cause of infant irritability in children with severe CHD remains unclear. It has been suggested that it may be related to the complex surgical intervention, repeated exposure to noxious stimuli during hospitalisation (hyperalgesia) and prolonged ICU and/or hospital length of stay (Torowicz et al., 2010).

The parents' behaviour towards their child plays a critical role in the child's development in infancy and toddlerhood. The quality of the parent–child relationship, in particular the responsiveness of the caregiving, affects brain growth and neuronal organisation. The quality of the caregiving therefore also influences social-emotional, cognitive and language development (Laing et al., 2010; Torowicz et al., 2010). Anxiety and depression in mothers can interfere with the quality and responsiveness of the parenting, negatively impacting on the child's development, especially cognitive development (Soulvie et al., 2012; Landolt et al., 2011; McCusker et al., 2009).

Family and maternal adjustment in particular play a central role in the behavioural outcomes of the children with CHD (McCusker et al., 2009). The child's unique characteristics, including temperament and health status, influence parenting practices in a child with chronic disease (Carey et al., 2002). Parents are often hyper-vigilant and overprotective of

their child who they see as vulnerable, resulting in so-called “vulnerable child syndrome” (Connor et al., 2010; Laing et al., 2010). Excessive parental concern and overindulgence can negatively influence the developmental outcome of these children over time. Parenting style tends to be more permissive, with a lack of discipline and failure to set boundaries (Vrijmoet-Wiersma et al., 2009; Brosig et al., 2007; Mussatto, 2006; Uzark and Jones, 2003; Carey et al., 2002). Mothers of children with CHD have also been found to have lower expectations of their children compared to mothers of healthy children (Brosig et al., 2007, Mussatto, 2006; Carey et al., 2002). Parents are often more sympathetic towards the child reinforcing illness behaviours, with the child becoming overly dependent, disobedient, irritable and uncooperative (Connor et al., 2010). This in turn influences developmental and behavioural outcomes of the child in the long-term (Vrijmoet-Wiersma et al., 2009; Brosig et al., 2007).

The parenting style described above has frequently been associated with behavioural difficulties in children (Laing et al., 2010). Behavioural difficulties in children with CHD have been directly related to the levels of parental stress and the burden of care (Vrijmoet-Wiersma et al., 2009; Mussatto, 2006).

2.6.2.6 Socioeconomic conditions and cost of care

Many families caring for a child with CHD experience financial strain and have been found to be financially unstable. Low SES and financial strain are stressors contributing to the psychological problems in parents of children with CHD (Grønning Dale et al., 2013; Harvey et al., 2013; Soulvie et al., 2012; Connor et al., 2010; Lawako and Soares, 2006). Living at lower socioeconomic levels is associated with more severe and numerous symptoms of depression in parents of children with CHD due to the difficulty in meeting the expensive and long-term care requirements (Yildiz et al., 2009).

Mothers, as primary caregivers, must often stay at home for extended periods of time to care for the ill child before cardiac intervention, and during the sometimes long recovery period post-cardiac intervention. This might result in mothers having to give up her employment or being unable to seek gainful employment during this period. The result being

reduced financial resources available to the family; limiting what they can afford (Bruce et al., 2014; Connor et al., 2010).

2.6.2.7 Low levels of parent education

Little has been reported in the literature on the effect of parental educational attainment on levels of parenting stress in children with CHD. Hearps et al. (2014) found that low levels of parental education increased psychosocial risk, increasing levels of parental stress. Yildiz et al.'s (2009) findings were at variance with the aforementioned, suggesting that parents' level of education did not have a significant effect on the level of stress experienced by parents. The true impact of parental educational attainment on levels of parenting stress remains poorly established and requires further investigation.

2.6.2.8 Family strain

Parenting a child with CHD comes at an emotional cost to the parents, but also to siblings and the rest of the family (Connor et al., 2010). Parents feel that the impact on siblings is a cause of considerable stress to them, and they experience guilt that they are neglecting their wellbeing (Bruce et al., 2014; Connor et al., 2010).The impact on members of the extended family can also be considerable. It may require family members to take time off work, assume childcare responsibilities for siblings, and assist the family financially (Connor et al., 2010).

2.6.2.9 Marital strain

Stress caused by having a child with CHD can place strain on a marriage. Marital unhappiness is considered a stressor for parents' psychosocial wellbeing (Grønning Dale et al., 2013; Yildiz et al., 2009; Goldberg et al., 1990). The impact of CHD on marital relationships in the available research is however inconclusive (Tak and McCubbin, 2002).

2.6.2.10 Lack of social support

Social support refers to the relationships parents have with other persons, including a spouse, other children, grandparents, friends, and colleagues who can provide emotional support (Bruce et al., 2014). Mothers who stay at home to care for the child with CHD may have few opportunities to participate in their social role, recreation and to socialise (Connor et al., 2010; Goldberg et al., 1990). The child's illness may force mothers into unwanted roles, limiting them to a lifestyle where they can rarely prioritise their own interests and social activities (Bruce et al., 2014; Connor et al., 2010).

Social support, social resources, social disadvantage, religion and family functioning have been identified as important indicators of psychosocial outcome in parents of children with CHD (Hearps et al., 2014). Mothers who experience role stress report inadequate social support. This lack of social support amplifies poor coping and serves as a stressor that may lead to psychosocial problems (Grønning Dale et al. 2013; Connor et al., 2010). Social isolation is associated with an increased risk of long-term psychosocial morbidity in parents of children with CHD (Srichantaranit et al., 2010; Vrijmoet-Wiersma et al., 2009; Mussatto, 2006).

2.6.3 Psychological morbidity in parents of children with congenital heart disease

It has been established that having a child with CHD has a profound negative effect on parental mental health (Grønning Dale et al., 2013). Psychological distress is an indicator of parents not coping and adjusting to their child's CHD (Fonseca et al., 2012; Connor et al., 2010). The effects of stressors are also cumulative over time (Fonseca et al., 2012). Although most parents show resilience in the face of the stressors caused by their child's CHD; a considerable number of families report persistent distress requiring psychosocial interventions (Hearps et al., 2014).

Parents of children with CHD report more psychological problems than parents of healthy children (Bruce et al., 2014; Fonseca et al., 2012; Vrijmoet-Wiersma et al., 2009; Yildiz et al., 2009; Mussatto, 2006) and children with other chronic diseases (Moola, 2012; Goldberg et al., 1990). As a consequence, parents may develop psychological symptoms, such as

stress, anxiety, depression and problems with coping and adaptation (Wei et al., 2016; Bruce et al., 2014; Soulvie et al., 2012; Solberg et al., 2011; Vrijmoet-Wiersma et al., 2009; Yildiz et al., 2009). Uzark and Jones (2003) suggested that as many as one in five parents of children with CHD exhibit clinically significant levels of stress.

Doherty et al. (2009) and Vrijmoet-Wiersma et al. (2009) reported that more than one-third of mothers of children with CHD met the criteria for poor adjustment and displayed clinically significant levels of stress. Soulvie et al. (2012) found elevated levels of psychological distress in 33% of parents with children with mild or moderate CHD, and in as many as 81% of mothers of children with severe CHD.

Lawoko and Soares (2006) reported on long-standing symptoms and psychosocial morbidity. They found that disease severity failed to explain parents' psychosocial morbidity over time. Instead, burden of care, social isolation, and financial instability were associated with an increased risk of long-standing psychological morbidity. Majnemer et al. (2006b) found that 25% of mothers' still experienced significant levels of stress five years after their child's cardiac surgery, while Hearps et al. (2014) reported that almost 40% of mothers were at risk of ongoing psychological problems.

2.6.4 Parenting stress outcomes in children with congenital heart disease

Very few studies have explored the experiences of parents who have had a child diagnosed with CHD and whose child had undergone cardiac surgery (Wei et al., 2016; Fonseca et al., 2012). Rempel et al. (2013) aptly described caring for a child with CHD as "parenting under pressure".

In their review of 25 studies on parenting stress in children with CHD, Soulvie et al. (2012) found that parents experienced increased levels of stress across the continuum of cardiac care. Studies by Bruce et al. (2014), Moola (2012), Fonseca et al. (2012) and Yildiz et al. (2009) similarly reported that parents of children with CHD experienced heightened levels of stress.

In contrast, Vrijmoet-Wiersma et al. (2009), Brosig et al. (2007) and Mussatto (2006) found that parents of children with CHD reported stress levels that were not significantly higher than those of parents of healthy children; in fact, in some instances parents of children with CHD reported lower stress levels than parents of healthy children. These lower stress levels could be explained by the fact that parents of children with CHD develop a higher threshold for what they perceive to be stressful, given their lived experiences. Parenting stress outcomes in the published literature suggest considerable variability in stress outcomes amongst individual parents.

Research has shown that parental stress levels decrease over time, after surgical intervention and with improvement of the child's condition (Moola, 2012; Landolt et al., 2011; Menahem et al., 2008). The majority of parents are able to adapt to caring for a child with CHD; however, almost 40% are at increased risk of psychosocial morbidity due to continued emotional stress. This may adversely impact on parental QOL and the capacity for optimal parenting (Hearps et al., 2014).

Improved social support has been found to mediate psychosocial distress. Family friends, an extended community and healthcare professionals can provide the necessary social support to parents. Increased opportunities for socialisation and physical exercise have also been shown to be beneficial for parents (Hartman and Medoff-Cooper, 2012; Lawoko and Soares, 2006). Most parents, despite the challenges faced by having a child with CHD, display the ability to cope, and are resourceful and resilient (Rempel et al., 2013). Wei et al. (2016) reported that over the long-term many parents view their child's CHD as a positive life experience that brought their family closer together.

2.6.5 Parenting stress outcomes in children with congenital heart disease and Down syndrome

Parental adaptation to having a child with DS has been studied extensively in relation to parental emotions and wellbeing. It has been found that parenting stress levels increase with the increasing age of the child with DS, and as developmental and behavioural problems became more apparent (Cuskelly et al., 2008). Parents of infants with DS have reported more stress than parents of infants without disabilities (Pelchat et al., 1999).

The aforementioned studies, however, did not take into account co-morbid medical problems in children with DS, such as CHD. Many children with DS also have CHD, and many more of these children are surviving making it increasingly important to evaluate the impact of CHD in addition to DS on family psychosocial functioning, including parenting stress and the impact on family life (Visootsak et al., 2015).

Visootsak et al.'s (2015) study is the only study to date that has evaluated family psychosocial outcomes associated with children with CHD with DS. They reported that the presence of CHD in addition to DS resulted in much greater levels of parenting stress than in cases where children were diagnosed with DS alone. Having a child with CHD in addition to DS was found to elevate parental concern and disrupt family dynamics, resulting in further neurodevelopmental deficits.

2.6.6 Parenting stress outcomes in resource-poor communities

It has been suggested that parenting stress is amplified by poor socioeconomic circumstances. There is little published data reporting on parental stress in children with CHD residing in poorer communities. In their study in the United Kingdom (UK), Franck et al. (2010) reported considerably higher levels of parenting stress in parents from poorer communities and where mothers were immigrants to the UK.

Amakali and Small (2013) investigated parenting stress in families of children with CHD in Namibia, a sub-Saharan African country. Most of the parents in their study had a low SES**.** Parents found parenting a child with CHD in these circumstances to be a greater challenge. Families who lived in rural communities had a greater burden of care in that they were expected to cope with all the care demands on their own. Most of the parents had low levels of education and as a result most had no steady income. A lack of financial means impeded access to the healthcare services that could have optimised the health and wellbeing of these children. Parents' poor coping and adaptation skills were found likely rooted in their lack of financial means to facilitate coping with the demands of care. Poor coping was further amplified in single parent and, female-headed households (Amakali and Small, 2013).

2.6.7 Parenting a child in a developing country

Parents in developing countries face multiple risks for psychosocial morbidity. Poverty and social disadvantage pose a considerable risk to parenting in SA (Gould and Ward, 2015, Ward et al., 2015; Cooper et al., 2009; Engle et al., 2007; Walker et al., 2007). A lack of financial resources does not only affect the ability of parents to provide nutrition and healthcare to their child, but also inherently makes parenting in itself more difficult (Gould and Ward, 2015). In addition, more than half of children in SA grow up in single parent-headed households, where the absent parent is largely uninvolved in the day-to-day parenting of the children (Gould and Ward, 2015). Parents living in poverty are also less likely to have the necessary social support that would assist them in their parenting role (Gould and Ward, 2015; Engle et al., 2007).

It has also been established that parents living in poverty are more likely to suffer from anxiety, stress and depression (Gould and Ward, 2015; Cooper et al., 2009; Walker et al., 2007). Cooper et al. (2009) reported that 34.7% of mothers in low-income peri-urban settings in SA suffer from depression. Walker et al. (2007) have even suggested that the prevalence of depression in mothers in developing countries may be as high as 60%.

Poverty and maternal depression severely compromises the ability of parents to provide the kind of childcare that promotes secure attachment in infancy, and the type of stimulation needed for optimal developmental outcome (Cooper et al., 2009). Maternal depression has been found to affect child-rearing practices in SA, in that depressed mothers have been found to be less involved, less sensitive and less responsive in their parenting style, resulting in them being more negative in their interactions with their infants (Walker et al., 2007).

2.6.8 Reducing psychosocial morbidity in parents of children with congenital heart disease: Implications for clinical practice

Routine screening of the psychosocial status and functioning of the family over the course of the child's cardiac care will assist in the identification of families at risk of psychosocial morbidity (Bruce et al., 2014; Hearps et al., 2014; Vrijmoet-Wiersma et al., 2009; Yildiz et al., 2009; Brosig et al., 2007; Mussatto, 2006; Carey et al., 2002). These parents should be

reffered for suitable interventions to reduce their stress (Soulvie et al., 2012; Mussatto, 2006), and help them to cope and adapt to their child's CHD and the subsequent lifestyle changes it demands (Wei et al., 2016; Bruce et al., 2014; McCusker et al., 2009; Yildiz et al., 2009; Lee et al., 2007; Lawoko and Soares, 2006).

Interventions may include educational, psychological and/or social support services (Rempel et al., 2013; Soulvie et al., 2012; Uzark and Jones, 2003). In addition, parent support groups may be beneficial in providing emotional support to parents (Bruce et al., 2014; Grønning Dale et al., 2013; Hartman and Medoff-Cooper, 2012; Solberg et al., 2011; Lee et al., 2007).

2.6.9 Summary

More parents than ever before are parenting children with CHD, and for many parents the experience of raising a child with CHD has proven to be challenging. Although little is known about how parents' wellbeing is affected by caring for a child with CHD, they are considered to be at risk of ongoing stress that over time may manifest as anxiety and depression. Parenting a child with CHD with DS is more stressful than parenting a child with CHD alone. Parents in developing countries such as SA face a multitude of stressors, in addition to the stressors related to their child's CHD, placing them at even higher risk of ongoing stress and depression. Poverty and social disadvantage pose a considerable risk to parenting in developing countries.

Families should be screened regularly for psychosocial risk as part of standard cardiac care. Where indicated, parents should be provided with anticipatory guidance, educational interventions and psychological support. Parent support groups may be valuable in mediating stress.

2.7. THE BURDEN OF CARING FOR A CHILD WITH CONGENITAL HEART DISEASE

2.7.1 Introduction

As a chronic health condition, the burden or cost of caring for a child with CHD is not only physical and emotional for parents, but also financial (Zarit et al., 1980). The financial cost of caring for a child with a chronic health condition is considerable, and may even be life-long (Connor et al., 2010; Gerber et al., 2010). Medical and other costs related to care begin almost immediately after birth for families of a child with CHD (Connor et al., 2010). Non-medical related factors, including SES and parental level of education, may influence both the survival and outcome of a child born with CHD (Kucik et al., 2014).

2.7.2 Financial burden of caring for a child with congenital heart disease

The financial cost of having a child with CHD is life-changing for many families (Raj et al., 2015). The continued care that is required may explain why the socioeconomic impact is so great (Kucik et al., 2014). Caregiving creates a financial burden for parents and, in many cases, the extended family. The increased financial burden may be the result of expenses related to the child's care and/or a loss of income (Girgis et al., 2013). In addition lower levels of income, educational attainment, and occupational prestige are associated with greater family instability, which increases the risk of parental separation and divorce (Conger et al., 2010).

Many families of children born with CHD experience a considerable decline in family income after having a child born with CHD. In many instances parents may have to give up their employment to take care of the ill child. This is especially true for mothers, who in most cases fulfil the role of primary caregiver. Caregiving reduces the likelihood of a parent being employed, and many caregivers are unable to work, need to take unpaid leave, have fewer work hours, are employed in lower paying jobs, or work from home to manage the demands of care (Raj et al., 2015; Girgis et al., 2013; Hoffman, 2013; Mughal et al., 2011; Connor et al., 2010; Gerber et al., 2010). This loss of income reduces the financial resources available to the family (Bruce et al., 2014).

For most parents the financial uncertainty of having to care for a child with a chronic health condition is a considerable burden to carry. The immediate and long-term out-of-pocket costs associated with caring for the child are often unpredictable (Raj et al., 2015; Mughal et al., 2011; Connor et al., 2010). The SES of families at diagnosis is associated with the extent of the financial strain experienced by families going forward. Middle and lower socioeconomic class families experience greater financial strain caused by unexpected out-of-pocket expenses (Connor et al., 2010).

In addition, financial strain placed on families during the hospitalisation of a child with CHD is often overwhelming (Raj et al., 2015). Unplanned out-of-pocket expenses during hospitalisation may include accommodation, food, transport and phone charges. Parents find these unplanned costs extremely stressful (Connor et al., 2010; Gerber et al., 2010). Having a child with more severe CHD is associated with even greater out-of-pocket costs incurred (Connor et al., 2010; Gerber et al., 2010).

Apart from the costs related to hospitalisation, out-of-pocket expenses for long-term follow-up are also considerable. These costs include transportation to and from the hospital for cardiac follow-up, and having to attend other services such EI services further increases the costs for families (Kucik et al., 2014; Amakali and Small, 2013; Hoffman, 2013; Gerber et al., 2010). The magnitude of the financial burden often results in families having to incur debt to cover out-of-pocket and monthly expenses (Raj et al., 2015; Amakali and Small, 2013; Connor et al., 2010).

Family income affects both the children's health and their access to healthcare (Kucik et al., 2014; Cassedy et al., 2013). Lower SES may negatively influence the ability of parents to seek out and access healthcare services (Kucik et al., 2014; Cassedy et al., 2013; Mughal et al., 2011). As a result socioeconomic disadvantage is associated with poorer survival and outcome in children born with CHD (Kucik et al., 2014; Cassedy et al., 2013), including adverse developmental outcomes (Conger et al., 2010). Income level is also associated with the quality of nutrition and the housing families can afford (Amakali and Small, 2013; Cassedy et al., 2013).

According to Hoffman (2013) poverty is considered one of the greatest barriers to the successful treatment of CHD in the developing world. The cost of chronic treatment in resource poor settings and the developing world is often higher due to late diagnosis and management of CHD, and the treatment of complications such as cardiac failure that would require frequent clinic visits adds to the economic strain experienced by the families in these settings (Sadoh et al., 2011).

Sadoh et al. (2011) found that in Nigeria over a third of families spent more than 10% of their monthly income on caring for the child with CHD (8% was spent on covering transport costs for medical care). This meant that families had less money available for necessities such as food, clothing and housing. Families from lower SES therefore proportionally spend more of their income on healthcare than would be the case in middle or upper class families.

According to Amakali and Small (2013) many families with children with CHD in sub-Saharan Africa live in rural areas and the parents have a low level of education resulting in them not being able to secure fixed employment. This resulted in no secure source of income and financial insecurity. Many of these families living in poverty were unable to provide the care necessary for a child with CHD. Dire financial situations also result in children missing healthcare appointments, as families cannot afford the transport costs to get them there. Financial problems have also been found to negatively impact parents' psychological functioning (Amakali and Small, 2013; Conger et al., 2010) and their QOL (Raj et al., 2015).

2.7.3 Educational attainment and the occupational prestige of parents

Family income, occupational prestige, and educational attainment serve as measures of SES and are considered to influence a person's life opportunities (Cassedy et al., 2013). According to Kucik et al. (2014) level of parental education serves as a proxy for health literacy and family income. These authors (Kucik et al., 2014) found that lower levels of maternal education were associated with poorer survival and outcome in infants with CHD. In addition, it was found that the SES and education level of the community in which these families lived also played an important role in survival and outcome.

2.7.4 Summary

The cost for families of caring for a child with CHD is not only physical and emotional, but also financial. The cost of caring for a child with a chronic health condition that requires ongoing medical care is considerable, and may potentially be life-long.

Many families of children born with CHD experience a considerable decline in family income as mothers take on the role of caring for the ill child full-time and therefore cannot be gainfully employed. In addition, the cost of travelling long distances to main city centres where cardiac units are located for follow-up and cardiac surgery are costly, with considerable out-of-pocket expenses for families such as accommodation, food and cellular phone charges, which add to the financial burden of families. As a result, many families face financial insecurity. The financial burden of care is amplified for parents living in developing countries where many families live in poor socioeconomic circumstances.

Family income, occupational prestige, and educational attainment are considered to serve as measures of the SES. Socioeconomic disadvantage is associated with poorer survival and outcome in children born with CHD, including worse developmental outcomes.

CHAPTER 3

OUTCOME MEASURES AND PILOT STUDY

In Chapter three the outcome measures used in this study will be described with regards to their purpose, content, administration and scoring. Standardisation, reliability and validity of the outcome measures will be highlighted. The use of each outcome measure in the SA population and in the CHD population will be justified.

The pilot study, which served to determine the feasibility of the study and the suitability of each of the chosen outcome measures, will also be described.

3.1 Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III)

3.1.1 Description of the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III)

The BSID-III is an individually administered instrument designed to assess the developmental performance of infants and young children aged one to 42 months (Bayley, 2006b). The BSID-III contains three administered scales, namely the cognitive scale, the language scale (including expressive and receptive language subtests) and the motor scale (including fine motor and gross motor subtests). The BSID-III also contains the social emotional and adaptive behaviour scales in the form of a parent self-report questionnaire (Bayley, 2006b). The social emotional and adaptive behaviour questionnaire was not utilised in this study, as its psychometric properties are not yet well established.

The BSID-III scales provide a comprehensive developmental assessment across the most important domains of childhood development. This contributes to the BSID-III's standing as

the “golden standard” measure for developmental assessment (Johnson et al., 2014; Marino et al., 2012).

The **cognitive scale** assess the child’s play (including play with objects, relational play and symbolic play), ability to process information (including novelty preference, habituation to visual and auditory information, paired comparisons, memory, problem solving, reaction time and anticipation of patterns), and number concepts and counting (Acton et al., 2011; Bayley, 2006b).

The **language scale** is comprised of a receptive communication subtest and an expressive communication subtest. The receptive communication subtest assesses the child’s auditory acuity, sound discrimination, verbal understanding, verbal concept development, and response to words and spoken requests (Acton et al., 2011; Bayley, 2006b). The expressive communication subtest on the other hand assess the child’s ability to vocalise and communicate via sounds, gestures and words (Bayley, 2006b).

The **motor scale** is comprised of a fine motor subtest and a gross motor subtest. The fine motor subtest assess the child’s co-ordination and control of eye movements, visual motor and visual spatial skills, and motor control of the hands (reach, grasp and manipulation skills) (Acton et al., 2011; Bayley, 2006b). The gross motor subtest assessing the child’s large body and complex movements as well as mobility. Motor development is assessed with increasing emphasis on the quality of movement (Acton et al., 2011; Bayley, 2006b).

3.1.2 Administration and scoring procedures for the BSID-III

No specific qualifications or training is required to administer the BSID. It is however recommended that clinicians who administer the BSID-III should be experienced in paediatric developmental assessment and interpretation (Albers and Grieve, 2007; Bayley, 2006a).

The child’s chronological age is calculated in years, months and days at the time of testing to determine the appropriate starting point for subtest administration. Where indicated, age

is to be adjusted for prematurity through 24 months chronological age. A child is considered premature if born at 36 weeks or less gestation (Bayley, 2006a).

Administration time for children under the age of 12 months is approximately 50 minutes and for children older than 13 months up to 90 minutes (Bayley, 2006a). Items are administered following the administration guidelines provided in the BSID-III administration manual. Items receive a score of one if the child meets the scoring criteria and, a score of zero if the criterion is not met (Bayley, 2006a).

Raw scores for each subscale are converted into composite scores (Bayley, 2006a) Composite scores are a transformation of the distribution of the scores and have a given mean and standard deviation. A score of 100 is the test mean score, and indicates average performance. Composite scores allow for the determination of the number of standard deviations the child's score is from the mean test score for all three subscales of 100 (Bayley, 2006b).

Table 3.1 shows the relation of composite scores to standard deviations from the mean.

Table 3.1 BSID-III composite scores and standard deviation equivalents

Composite score	Standard deviation from the mean
55	-3
70	-2
85	-1
100	0
115	+1
130	+2
145	+3

(Bayley, 2006b, p109).

Composite scores can be described in more qualitative terms in accordance with the child's level of developmental performance (Bayley, 2006b). Descriptive classifications for the composite scores are provided in Table. 3.2 (Bayley, 2006b).

Table 3.2 Descriptive classifications of the BSID-III composite scores

Score	Performance category
130 and above	Very superior
120 - 129	Superior
110 - 119	High average
90 - 109	Average
80 - 89	Low average
70 - 79	Below average
69 and below	Extremely low

(Bayley, 2006b, p113).

For the purpose of this study, the same descriptive classification system as described by Mussatto et al. (2014), based on the standard deviations of the composite scores from the mean test score, will be used to allow for comparison of developmental outcomes between studies. Developmental performance is to be classified as “average” if the score is within one SD of the mean or higher (scores > 85), “at risk” if the score is between one and two SDs below the mean (scores of 70–84), and “delayed” if the scores are more than two SDs below the mean (scores <70).

3.1.3 Standardisation and norming of the BSID-III

The clinical use of the BSID-III was improved during its standardisation through the numerous special population studies undertaken in children diagnosed with developmental delay, at risk of developmental delay (including those born prematurely and those with genetic or congenital disorders) and/ or a clinical diagnosis (for example DS, cerebral palsy and birth asphyxia) (Bayley, 2006b). The BSID-III was normed in a stratified, random sample of 1700 children representative of children aged 16 days to 42 months in the US (Bayley, 2006b).

3.1.4 Reliability and validity of the BSID-III

The BSID-III has been proven a reliable measure, which suggests that the test scores are accurate, consistent and stable. Evidence of the internal consistency of the BSID-III composite scores has been shown with reliability coefficients of .91 for the cognitive scale,

.93 for the language scale, and .92 for the motor scale respectively (Bayley, 2006b). The reliability coefficients for special populations (as outlined under 3.1.5) support the generalisability of the instrument (Bayley, 2006b). The BSID-III has also been shown good test-retest stability over time (Bayley, 2006b). The BSID-III has also shown good content and construct validity (Bayley, 2006b).

3.1.5 Concerns regarding the BSID-III

Despite the extensive use of the BSID-III in both the clinical and research setting, there are published concerns that the BSID-III overestimates developmental performance (Johnson et al., 2014; Jary et al., 2013; Bos, 2013; Moore et al., 2012; Lowe et al., 2012; Vohr et al., 2012; Acton et al., 2011; Anderson et al., 2010). This could affect the interpretation of test results, with further implications in both the clinical and research setting (Acton et al., 2011; Anderson et al., 2010). Research in various populations has found that the BSID III identifies fewer children with scores of less than 70 than the BSID-II. Overestimation of developmental performance could result in children who have developmental delay not being identified (Jary et al., 2013; Moore et al., 2012; Vohr et al.; 2012; Acton et al., 2011). Test performance is also used to determine the need for referral to EI services. This would mean that some children who should be referred for early developmental intervention would not be referred, potentially impacting on their long term developmental outcome (Johnson et al., 2014; Vohr et al., 2012; Anderson et al., 2010).

Concerns regarding language, and cultural biases contained in the BSID-III have also been noted (Acton et al., 2011). Linguistic bias is of concern in children who do not learn and speak English as a first language (Madaschi et al., 2016; Paradis, 2005). SES could affect language performance, with children from poorer socioeconomic backgrounds and parents with lower levels of education exposed to far fewer words. Children with better socioeconomic backgrounds may therefore have an advantage on the assessment because of their more extensive vocabularies (Risley and Hart, 2006).

Prior experience with test content and the testing environment may affect a child's performance on the BSID-III. The test may contain tasks that the child is not exposed to in their culture or environment. Furthermore, a child's performance may be affected by their

exposure to books (Pēna and Quinn, 1997). Test items on the language subscale also do not consider socialisation practices. The child's interaction with the examiner during the test may be influenced by cultural experiences and practices (Pēna and Quinn, 1997).

The entire test battery and duration of the test requires considerable attention. If the child is unmotivated, disinterested and does not pay adequate attention during the test he/she may underperform and the results may not be a true indication of the child's capability. In addition fatigue may play a role in performance (Columbia University Leaders Project, 2013).

3.1.6 Use of the BSID-III as a measure of development in the South African population

The BSID-III has only been used in a handful of clinical studies in Africa and SA to date. No published norms for the BSID-III in African countries are currently available (Hutchings and Potterton, 2014). The BSID-III was found to be a valid measure of infant development in South Africa (Rademeyer and Jacklin, 2013), and has been used in studies on children with low birth weight (Ballot et al., 2012), Down syndrome (Russell et al., 2016) and HIV (Whitehead et al., 2014; Hutchings and Potterton, 2014). Scant information was provided by the aforementioned authors on any challenges of using the BSID-III in the SA context.

3.1.7 Use of the BSID-III as a measure of development in children with congenital heart disease

The AHA guideline on the evaluation of development in children with CHD indicates the BSD-III to be the outcome measure of choice for evaluating development in infants and toddlers (Marino et al., 2012). Only eight cardiac neurodevelopmental outcome studies have so far made use of the BSID-III. These included studies by Alsaied et al. (2016), Mussatto et al. (2015); Mussatto et al., (2014), Beca et al. (2013), Brosig Soto et al. (2011), Acton et al. (2011), Long et al. (2012a) and Visootsak et al. (2011). All of the aforementioned authors found the BSID-III to be a valid measure of developmental outcome in children with CHD. No mention was made of any specific challenges in using the measure in children with CHD. To date, the BSID-III has not been used to determine developmental performance in children with CHD in Africa.

3.1.8 Permission to use the BSID-III

Pearson Inc. granted written permission for the use of the test in its as-published formats for this research thesis. (See Appendix III for the user agreement with Pearson Inc.).

3.2 Parenting Stress Index Short Form (PSI-SF)

3.2.1 Description of the PSI-SF subscales

The PSI-SF (Abdin, 1995) is a self-report measure that measures parental stress across three subscales. The “parenting stress (PS)” subscale determines the extent of the distress a parent experiences in his/her role directly related to parenting a child, whilst the “parent-child dysfunction(P-CDI)" subscale looks at parents perception that his/her child does not meet their expectations. The “difficult child (DC)” subscale focuses on the behavioural characteristics of the child that make them either easy or difficult to parent (Abdin, 1995).

The theoretical model for the PSI-SF as developed by Abdin (1995) is depicted in Figure 3.1.

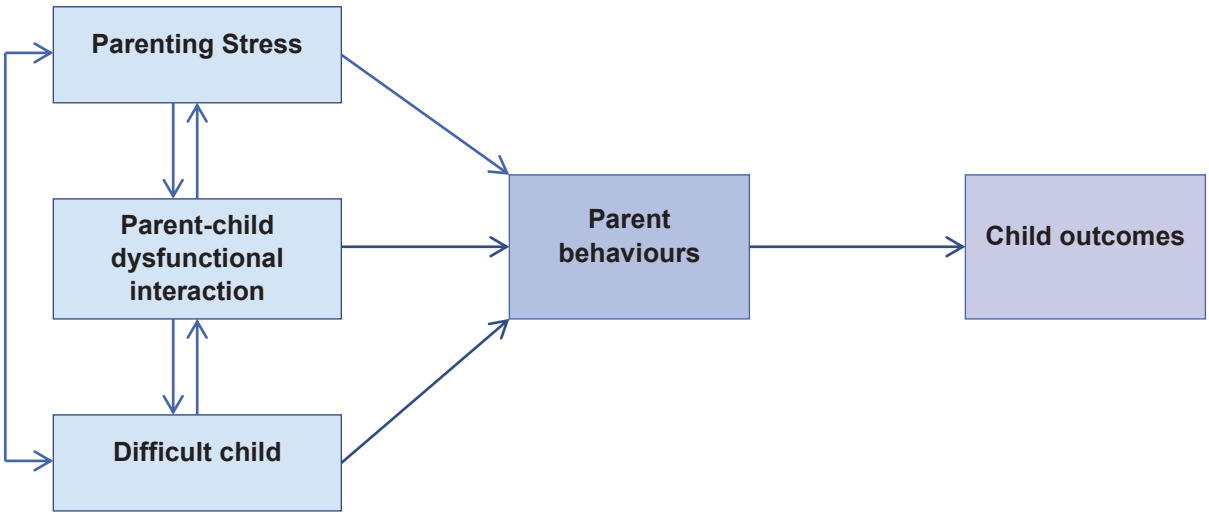

Figure 3.1 Theoretical model of the PSI-SF (Abdin, 1995, p 54).

3.2.2 Administration and scoring of the PSI-SF

No specific professional qualifications or training is required to administer or score the PSI-SF. The Parenting Stress Index (PSI) manual does however recommend that the interpretation of the PSI-SF scores require graduate training in clinical psychology or a related medical field (Abdin, 1995).

On average it should not take a parent more than ten minutes to complete the PSI-SF. (Abdin, 1995). Parents make use of a five-point Likert scale to indicate the extent to which they agree or disagree with each statement. “Strongly agree” is scored a 5, “agree” a 4, “not sure” a 3, “disagree” a 2 and “strongly disagree” a 1 (Abdin, 1995). The scoring sheet is then used to calculate a total score for each subscale. A total stress score is calculated by adding the scores from the three subscales. Raw scores are then converted into percentiles (Abdin, 1995). Normal scores lie between the 15th and 80th percentile. Scores are considered to be high if they are above the 85th percentile, and clinically significant if above the 90th percentile. A high score on any of the subscales is indicative of increased levels of parenting stress (Abdin, 1995).

3.2.3 Standardisation and norming of the PSI-SF

The PSI has been standardised for use in a stratified sample of parents of children between the ages of one month and 12 years (Abdin, 1995). The PSI was normed in a sample in the US consisting of 2 633 mothers of children ranging in age from one month to 12 years, and in 200 fathers of children aged six months to six years (Abdin, 1995). The PSI-SF was developed by means of a series of factor analyses of the PSI done in two samples of 530 and 270 mothers respectively in the US (Abdin, 1995).

3.2.4 Reliability and validity of the PSI-SF

The PSI-SF is feasible to use in a busy clinical setting and was specifically designed for administration under time constraints (Abdin, 1995). The PSI-SF has been shown to be a reliable measure with test-retest reliabilities of .84 for total stress, .85 for PD, .68 for P-CDI,

and .78 for DC respectively. The alpha internal reliability coefficients for total stress were .91 for total stress, .79 for PD, .80 for P-CD and .78 for DC respectively (Abdin, 1995).

The PSI has been shown to have good construct and predictive validity; there is however no body of independent research to show the validity of the PSI-SF. The PSI-SF has been shown to strongly correlate with the PSI on the total stress score with a correlation of .94. As the PSI-SF is a direct derivative of the PSI it is most likely that it will share the same validity. The PSI has been used in various non-English speaking cultures and had been shown to maintain its validity (Abdin, 1995). Studies by Pérez Padilla et al. (2015), McKelvey et al. (2009), Haskett et al. (2006) and Reitman et al. (2002) have supported the validity of the PSI-SF.

3.2.5 Use of the PSI-SF as a measure of parenting stress in the South African population

The PSI-SF has been used in a very limited number of clinical studies in SA including in parents of children with HIV (Verster, 2010; Potterton et al., 2007) and cerebral palsy (Pugin, 2007), and in mothers with substance abuse problems (Miles, 2007). The aforementioned studies all found the PSI-SF to be a valid measure for determining parental stress in the South African population.

3.2.6 Use of the PSI-SF as a measure of parenting stress in children with congenital heart disease

Studies by Visootsak et al. (2015), Vrijmoet-Wiersma et al. (2009), Lee et al. (2007), Uzark and Jones (2003), Carey et al. (2002) and Goldberg et al. (1990) made use of the PSI-SF to determine levels of parenting stress in parents of children with CHD. These studies found the PSI-SF to be a valid measure for establishing parental stress in this population.

3.2.7 Permission to use the PSI-SF

The distributor of the PSI, Psychological Assessment Resources Incorporated (PAR), granted the researcher permission to use the PSI-SF for this study. (See Appendix IV for user agreement with Psychological Assessment Resources, Inc.)

3.2.8 Translation of the PSI-SF

The PSI-SF is available in English and Sesotho. The complete PSI has been translated into Afrikaans. The distributor of the PSI, Psychological Assessment Resources Incorporated (PAR-Inc.), granted the researcher permission to extract the 36 items contained in the PSI-SF from the full Afrikaans version of the PSI for the purpose of this study.

3.3 Paediatric Quality of life Inventory™ (PedsQL™)

3.3.1 Development of the Peds QL™

The PedsQL™ is a modular measure developed to measure HRQOL in healthy children, as well as those with chronic diseases. Disease-specific modules serve to determine the impact of disease and its treatment on the child's function and ability to derive satisfaction in various aspects of life, including physical, psychological and social domains (Varni et al., 2011, Varni et al., 2007).

3.3.2 Description of the PedsQL™ scales and modules used

As children aged 36 months and younger were included in this study, the PedsQL™ Infant Scales (1-24 months) and PedsQL™ 3.0 Cardiac Module for toddlers (2-4 years) were chosen as the outcome measures for HRQOL. There is no PedsQL™ cardiac module available for children younger than two years. Uzark et al. (2003) however found that the PedsQL™ Generic Core Scales and the Cardiac Modules showed a significant correlation.

3.3.2.1 PedsQL™ Infant Scales

The PedsQL™ Infant Scales contain two age-appropriate versions, namely for infants aged one to 12 months and infants aged 13 to 24 months. The PedsQL™ Infant Scale is proxy-rated, and parents report on their perceptions of their child's HRQOL (Varni et al., 2011, Goldbeck and Melches, 2005; Raat et al., 2006). The PedsQL™ Infant Scales contains items over five scales include physical functioning, physical symptoms, emotional functioning, social functioning, and cognitive functioning (Varni et al., 2011).

3.3.2.2 PedsQL™ 3.0 Cardiac Module

The Paediatric Quality of Life Inventory (PedsQL™) 3.0 Cardiac Module has been designed as a disease-specific module that serves to evaluate HRQOL in children with cardiac disease from the age of two years (Berkes et al., 2010; Uzark et al., 2003). The PedsQL™ 3.0 Cardiac Module covers five scales relating to symptoms, perceived physical appearance, treatment anxiety, and cognitive and communication problems (Uzark et al., 2003).

3.3.3 Administration and scoring of the PedsQL™

No specific professional qualifications or training is required to administer the PedsQL™. In the case of parents completing the PedsQL™ questionnaire, administration should not exceed five minutes (Varni et al., 1999). Parents are asked how much of a problem each item has been during the past one month. A five-point Likert response scale is used, where 0 is "never a problem", 1 is "almost never a problem", 2 is "sometimes a problem", 3 is "often a problem", and 4 is "almost always a problem" (Varni et al., 2011; Uzark et al., 2003).

3.3.3.1 Scoring of the PedsQL™ Infant Scales

Items are reverse scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0). Higher scores indicate better HRQOL. Scale scores are computed as the sum of the items divided by the number of items answered. The total scale score is computed as the sum of all the items on the PedsQL™ Infant Scales divided by the number of items answered (Varni et al., 2011). The physical health summary score is calculated as

the sum of the items over the number of items answered in the physical functioning and physical symptoms scales. The psychosocial health summary score is calculated as the sum of the items over the number of items answered in the emotional, social, and cognitive functioning scales (Varni et al., 2011).

3.3.3.2 Scoring of the PedsQL™ 3.0 Cardiac Module

Items are reverse scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0). Higher scores indicate better HRQOL. Scale scores are computed as the sum of the items divided by the number of items answered. No total scaled score is computed for PedsQL™ Cardiac Module (Uzark et al., 2003).

3.3.4 Standardisation and norming of the PedsQL™

PedsQL™ Infant Scales were tested in a stratified sample of 420 parents of infants aged one to 12 months, and in 263 parents of infants aged 13 to 24 months across the US (Varni et al., 2011). Uzark et al. (2003) administered the PedsQL Generic Core Scales and Cardiac Module to 250 children aged five to 18 years, and in 344 parents of children aged two to 18 years with cardiac disease at the Cincinnati Children's Hospital in the US.

3.3.5 Reliability and validity of the PedsQL™ Infant Scales and Cardiac Module

Varni et al. (2011) established that the PedsQL™ Infant Scales is a feasible measure to determine the HRQOL of infants. They found the measure showed very few missing item responses. The alpha reliability coefficient for the PedsQL™ Infant Scale is .92. The PedsQL™ Infant Scale was also shown to have good discriminative validity in that it could differentiate between healthy and ill infants.

Uzark et al. (2003) established that the PedsQL™ 3.0 Cardiac Module is a feasible measure to determine HRQOL of toddlers with CHD. They found the measure showed few missing item responses. The alpha reliability coefficient for the PedsQL™ 3.0 Cardiac Module was .93. The PedsQL™ 3.0 Cardiac Module also showed good construct validity and scores across the five scales, and correlated with scores on the PedsQL™ 4.0 Generic Core Scale

scores.

3.3.6 Use of the PedsQL™ as a measure of health-related quality of life in the South African population

The PedsQL™ has only been used in a limited number of clinical studies in SA to investigate HRQOL in children with HIV (Goldberg, 2011), brain tumours (Penn, 2013) and post-burn (Weedon and Potterton, 2011). The aforementioned studies have shown the Peds-QL™ to be a feasible, reliable and valid measure for HRQOL outcomes in varied paediatric populations in SA.

3.3.7 Use of the PedsQL™ as a measure of health-related quality of life in children with congenital heart disease

No studies could be found that report on the HRQOL outcomes of children aged two years and younger with CHD using the PedsQL™ Infant Scales. However, the PedsQL™ infant modules have been successfully used to establish HRQOL in children younger than two years with other chronic diseases such as chronic liver disease (Mohammed et al., 2016).

Studies by Uzark et al. (2003), Pike et al. (2007), Uzark et al. (2008), Berkes et al. (2010),Tahirović et al. (2010) and Eagleson et al. (2013) have reported on the HRQOL outcomes of children aged two years and older with CHD using the PedsQL™ 3.0. Cardiac Module. All of the aforementioned studies found the PedsQL™ 3.0 Cardiac Module to be a feasible, valid and reliable measure of HRQOL in children with CHD aged two years and older. No studies have however been conducted in SA using the Peds-QL™ as a measure of HRQOL outcomes in the paediatric cardiac population to date.

3.3.8 Permission to use the PedsQL™

A user agreement was signed with Mapi Research Trust, Lyon, France, prior to use the questionnaires. This included the PedsQL™ Infant Scales (1-12 months) and (13-24 months) and the PedsQL™ Cardiac Module (2-4 years). (See Appendix V for the user agreement with Mapi Research Trust).

3.3.9 Translation of the PedsQL™

The PedsQL™ Infant Scales (1-12 months) and the PedsQL™ Infant Scales (13-24 months) were available from the distributor in English, Afrikaans and Sesotho (Varni, 2013).

The PedsQL™ Cardiac Module (2-4 years) was only available in English, and was translated into Afrikaans and Sesotho in line with the stipulated prescripts of the distributor prior to the commencement of the study (Varni, 2013). Further language validation of the translations was not possible as the translated questionnaires were not utilised during this study due to the age range of the participants and the caregiver's language preferences, which failed to provide the opportunity to do so.

3.4 Hollingshead Socioeconomic Index and Hollingshead Index of Social Position

3.4.1 Determinants of Hollingshead's Four Factor Index of Social Status

Hollingshead's Four Factor Index of Social Status calculates social status by collecting information on four factors, namely education, occupation, gender and marital status (Hollingshead, 1975).

3.4.2 Calculation and interpretation of the Hollingshead indices

3.4.2.1 Hollingshead Socioeconomic Index

Each parent's educational level is rated on a seven point scale according to the highest grade completed and each parent's occupational level is rated on a nine-point scale (Hollingshead, 1975). The SES index score for each parent is calculated using a weighted formula where occupation is weighted 5 and education is weighted 4 (Hollingshead, 1975).

Adding the status score of the mother and the status score of the father and dividing it by two calculates the socioeconomic status score for the family. This score is then used to determine the family's social strata. Table 3.3 presents the socioeconomic index and social class equivalents of the Hollingshead Socioeconomic Index.

Table 3.3 Social class according to the Hollingshead Socioeconomic Index scores

Socioeconomic index score	Social class equivalent
55 – 66	Major business or professional
40 – 54	Medium business or minor professional
30 – 39	Clerical worker or craftsman or sales worker
20 – 29	Machinist or semi-skilled labourer
9 -18	Unskilled labour or menial worker

(Hollingshead, 1975, p 18)

3.4.2.2 Hollingshead Index of Social Position

The Hollingshead Index of Social Position (ISP) is a two-factor index calculated using a weighted formula where occupation is weighted 7 and education is weighted 4 (Lantos, 2015). A score for each parent is calculated. The score for each parent is added and divided by two to get the ISP score for the family. The score is then used to assign families to a social class category. Table 3.4 presents the ISP score and the social class equivalent of the Hollingshead ISP.

Table 3.4 Social class categories for the Hollingshead Index of Social Position scores

ISP score	Social class equivalent
11 – 17	Upper class
18 – 31	Upper-middle class
32 - 47	Middle class
48 - 63	Lower –middle class
64 - 77	Lower class

(Lantos, 2015, p227)

3.4.3 Reliability and validity of the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position

The Hollingshead Socioeconomic Index still lacks evidence of reliability and validity. However, according to experts in social stratification, it remains the index that other indices are benchmarked against (Cassedy et al., 2013). It remains the only outcome measure of

SES reported in the published CHD literature. Thus, this measure was still chosen for this study, despite its limitations, as it allowed for direct comparisons between studies.

3.4.4 Use of the Hollingshead Socioeconomic Index and Hollingshead Index of Social Position as a measure of social status in the South African population

The Hollingshead Socioeconomic Index, as a measure of socioeconomic and social status, has not been widely used in South African healthcare research. Two studies were identified to have used the Hollingshead Socioeconomic Index. Simelane (2015) studied the impact of SES on parenting autistic children in SA, while Bogart et al. (2013) investigated the role of parents in a HIV prevention programme in adolescents.

3.4.5 The Hollingshead Socioeconomic Index and Hollingshead Index of Social Position as a measure of social status in families of children with congenital heart disease.

Varni et al. (2007) included the Hollingshead Socioeconomic Index as a measure of social status in their family information form, contained in the PedsQL^{TM} Generic Core Scales which is used to determine HRQOL in children. The Hollingshead Socioeconomic Index has been used in several paediatric cardiology studies to determine the SES of families including studies by Connor et al. (2010), Uzark et al. (2008) and Cassedy et al. (2013).

3.4.6 Concerns regarding the Hollingshead Socioeconomic Index and the Hollingshead Index of Social Position

Concerns have been expressed as to whether the Hollingshead Socioeconomic Index and the Hollingshead Index of Social Position are adequate measures of social status. The biggest concerns with the measure is that social status is determined by education and occupation. Occupational prestige might not only depend on the type of occupation, but the aspects of the occupation itself. Hollingshead also assumed that income was linked to education and occupation, which might not always be the case. Despite the possible limitations the Hollingshead Socioeconomic Index is still widely used in healthcare research (Cassedy et al., 2013; Weakliem and Adams, 2011).

3.4.7 Permission for use of the Hollingshead Socioeconomic Index and the Hollingshead Index of Social Position

There is no restriction on the use of Hollingshead Socioeconomic Index and the Index of Social Position (ISP). The respective formulas for the calculations are freely available online in Hollingshead's (1975) unpublished manuscript and from Lantos (2015) respectively.

3.5 Pilot study

The researcher performed multiple developmental assessments on high-risk children aged between one and 42 months in the months prior to the commencement of the study in order to familiarise herself with the subtests, testing and scoring procedures, and test items contained in the BSID-III. This served to improve the accuracy of the developmental assessments during the pilot study, as well as the main study. Once ethical clearance was attained, the study was piloted in line with the approved protocol (Refer to 4.6 for the study procedure followed). Six children meeting the inclusion criteria were included in the pilot study (10% of the anticipated study sample).

The pilot study served multiple purposes, including the determination of the feasibility of this study. Another important purpose of the pilot study was to determine the suitability of the chosen outcome measures for the purpose of this study and in the identified population. Although all chosen outcome measures have been used in similar studies in young children with CHD in developed countries and in paediatric populations in SA, none had been used in the paediatric CHD population in SA before. All outcome measures were found to be suitable for use in the population of young children with CHD in central SA during the pilot study.

The pilot study allowed for a review of the logistical aspects around the physical assessment of the children, and the interview and completion of the questionnaires with the parents in the paediatric cardiothoracic ward, cardiology unit and physiotherapy department at Universitas Academic Hospital in Bloemfontein, Free State. The researcher had not previously assessed and treated children with CHD in the cardiothoracic ward and cardiology unit. The cardiothoracic ward and cardiology unit were however chosen as the

site for the baseline assessments for logistical reasons, as the children needed to be accessible to both nursing staff and doctors for routine procedures on the afternoon of the day before their scheduled cardiac intervention.

Performing the baseline assessments in the cardiothoracic ward and cardiology unit proved to be a challenge with regard to finding a quiet and private area or room in which to conduct the interviews with the parents, complete the self-administered questionnaires, and to do the children's developmental assessment in a busy clinical setting. The pilot study allowed the researcher to identify the most suitable areas in each ward for this purpose, being either the consultation room or the patient's own room. Unfortunately, as these were both busy clinical wards, the consultation room was at times in use by other clinicians, which required the need for improvisation and flexibility with regard to the assessment venue. Parent interviews were always conducted in a private consultation room to ensure confidentiality. The private consultation room was equipped with a table and chairs for the completion of the questionnaires and there was sufficient space to do the BSID-III assessment. If the consultation room was unavailable at the time of the developmental assessment, the assessment was done in the patient's room. A therapy mat, child-sized table, chairs and a stairs were available in the ward for the developmental assessments.

The physiotherapy department availed a private paediatric outpatient area with all the necessary equipment to the researcher for use by her for all the three-month and six-month follow-up assessments. The original plan was to do the follow-up assessments in the paediatric clinic at Universitas Academic Hospital where the cardiology clinic was held. However, this was not feasible due to the lack of space in the busy clinic. All follow-up visits were held in the physiotherapy department, and the researcher accompanied parents and children from the cardiology clinic to the physiotherapy department in order to ensure that they were not lost between the two sites.

The pilot study showed the researcher to be proficient in the administration of the PSI-SF and PedsQL™. It came to light during the pilot study that parents lacked the confidence to complete the self-administered questionnaires on their own, preferring the researcher to sit with them during the completion so as to clarify any uncertainties. It was found that the suggested timeframes for the self-administered questionnaires greatly exceeded the

suggested five to ten minutes per questionnaire. This resulted in having to allow for closer to 20 minutes per questionnaire in the main study. In the case of Sotho-speaking mothers, a translator was also present to assist with translation and clarification when required. In cases where a translator was used, up to 25 minutes per questionnaire had to be allowed for in the main study. The developmental assessment took between 60 and 90 minutes, as suggested in the technical manual of the BSID-III, and the test duration was influenced by the child's age, with older children taking longer to assess.

The pilot study assisted the researcher in determining a logical sequence for the assessment. The administration guidelines for the self-administered questionnaire recommend that they be administered first before further assessments. This was however not found to be feasible in this study, in particular at baseline. Children undergoing cardiac surgery were in most cases admitted to the cardiothoracic ward after midday on the day before their surgery. Being admitted in the afternoon on the day before surgery posed a considerable challenge relating to time, in that these children still had to undergo multiple routine medical examinations and routine tests before their surgery. It was not possible to have the children admitted earlier as this would mean that they would have to have been admitted the previous week and remain in hospital over the weekend, resulting in an increase in hospital costs and inconvenience for the families. In most cases, this left the researcher with limited time available in which to complete the baseline assessment before the child became too tired and irritable. The priority at baseline was to complete the child's physical examination and developmental assessments first; this included the neurological examination, measurement of head circumference and length, and the BSID-III. The self-administered questionnaires were completed directly after the child's assessment; and where not possible, the questionnaires could be completed in the morning on the day of the child's surgery. It was decided that the same routine was to be followed at the three-month and six-month visits to ensure a consistent procedure for the children and parents. The time frame required for each assessment in total was determined to be between 90 and 120 minutes.

No changes were made to the study procedures, and the quality of the assessments done in the pilot study were such that the researcher included all the data collected in the pilot study in the main study.

3.6 Conclusion

Based on the extensive literature review and the findings from the pilot study the BSID-III, PSI-SF, PedsQL™ and the Hollingshead Socioeconomic Index were deemed suitable outcome measures for use in this study.

The method for Phase I and II of this study will be presented in Chapter four.

CHAPTER 4

METHOD FOR PHASE I AND II

In this chapter, the methodology for Phase I and II of this study is presented. The study design and participant recruitment is described and the study procedure will be outlined.

4.1 Study location

The study was conducted at the Paediatric Cardiology Unit located at the Universitas Academic Hospital in Bloemfontein.

The Paediatric Cardiology Unit at Universitas Academic Hospital services the population of central SA, estimated to be 4.2 million people. Central SA for the purpose of paediatric cardiology services in SA refers to the Free State and Northern Cape provinces, as well as the neighbouring country of Lesotho (Hoosen et al., 2010a). In addition, a number of children residing in the Eastern Cape are also treated at the Bloemfontein unit. Figure 4.1 provides a geographical view of the provinces of SA. The most frequently treated congenital heart defects at this unit include VSD, AVSD and PDA.



Figure 4.1 Map of the provinces of South Africa (Google images)

On average six to seven children, 30 months and younger, underwent cardiac surgery per month at Universitas Academic Hospital at the time of the study. Children only had access to mechanical ventilation as a form of mechanical circulatory support. ECMO and VAD mechanical circulatory support technologies were not available to these children.

4.2 Ethical considerations

Ethical clearance was obtained for this study from the Ethics Committee of the Faculty of Health Sciences, University of the Free State (clearance certificate number ECUFS 177/2013) and the Committee for Research on Human Subjects, University of Witwatersrand (clearance certificate number M131056) prior to the commencement of the study. (See Appendix VI for the ethical clearance certificates).

Permission to conduct the study was obtained from the relevant authorities at Universitas Academic Hospital, including the Clinical Manager, the Head of the Department of Cardiothoracic Surgery Department and the Head of the Department of Paediatric Cardiology. (See Appendix VII for the permission letters from the relevant authorities). The

Physiotherapy Department at Universitas Academic Hospital granted permission for the use of a venue within the Department for all three-month and six month follow-up assessments.

Participants in Phase I and Phase II of the study included both children and their parents. Parents were informed of the purpose of the study by means of an information letter, and the researcher provided further verbal explanation where necessary (a translator was used to assist in the case of Sesotho-speaking parents). Written informed consent was obtained from parents for their personal participation in the study. As the study also included their young children, who were incapable of providing informed consent, parents also provided written permission for their children's participation in the study (PAREXEL International, 2010; RSA-DoH, 2006). (Refer to Appendix VIII for the parent information letter and informed consent form for Phase I and II).

A contribution was made towards the transportation costs incurred by the participants for their attendance of both the three-month and six-month follow-up visits. This was done in accordance with the National Human Research Ethics Council of SA (NHREC) guidelines (2012) on the payment of study participants in SA.

The study was conducted in line with the approved protocol. Participation in this study was voluntary. Parents had the right to decline participation or withdraw from the study with their child at any point without reason or risk of penalty or discrimination. Children continued to receive standard cardiac care irrespective of their participation in the study.

Cardiac neurodevelopmental follow-up is not offered as part of standard care at the Cardiology Unit at Universitas Academic Hospital. Where indicated, the researcher referred children who qualified for EI therapy services (included PT, OT and ST) based on their developmental performance to their nearest service point.

4.3 Study design

Phase I and II of the study made use of an observational descriptive study design.

4.4 Participants

The study population consisted of young children with CHD and their parents who attended the Paediatric Cardiology Unit at Universitas Academic Hospital in Bloemfontein. For the purpose of this study, young children will refer to infants (1 month to 1 year) and toddlers (1 year to 3.5 years) (Marino et al., 2012).
All children aged 30 months and younger, who met the inclusion criteria, were recruited into the study. Parents who granted written informed consent for their personal participation, as well as written permission for their child's participation, were included in the study sample.

The inclusion and exclusion criteria were set as follows:

Inclusion criteria:

- Children 30 months and younger at the time of inclusion.
- Children diagnosed with a congenital heart defect that required cardiac surgery.
- Attended cardiac services with a parent who could speak English, Afrikaans or Sesotho.
- Parents had to be willing to attend scheduled follow-up visits with their child over a six-month period.

Exclusion criteria:

- Children who were critically ill and could not be accurately and/or safely assessed.
- Neonates (children younger than 28 days).
- Children who had undergone previous or emergency cardiac surgery.
- Children who only underwent interventional cardiac catheterisation.
- Parents who declined to participate in the study, and/or were unwilling to grant permission for their child's participation.
-

As congenital heart disease is a rare disease, a sample of convenience was used during Phase I and Phase II of the study due to the small study population. Forty consecutive participants were included in Phase I of the study and 22 participants exited the study at the

end of Phase II. Six participants died post-cardiac surgery (15% mortality rate) and a further twelve participants (30%) were lost to follow-up by the end of Phase II (Refer to Figure 4.2 for a flow diagram depicting the study procedure).

4.5 Materials and measurements

The evidence-based guidelines for neurodevelopmental evaluation for infants and toddlers, provided in the scientific statement from the AHA on the evaluation and management of neurodevelopment in children with CHD (Marino et al., 2012), were taken into consideration when deciding upon the content of the neurodevelopmental assessment in this study. Based on their recommendation the BSID-III was chosen as the standardised developmental outcome measure. In addition growth parameters were measured (height, weight and head circumference) and a neuromotor examination (muscle tone and deep tendon reflexes) performed.

4.5.1 Demographic information of the child and family

Demographic information of the child with regards to age, gender, ethnicity and birth history (birth date, gestational age, birth weight and Apgar scores) was collected at baseline (See Appendix IX). Ethnic groups were identified in accordance with the 2011 South African Census as black African, Coloured, Indian or Asian, white and other (Statistics South Africa, 2012). Parents selected the ethnic group with which they personally identified.

Demographic information of the family with regards to the primary caregiver of the child, residence, mother's age, number of siblings and teratogens was collected at baseline (See Appendix IX).

4.5.2 Socioeconomic status of the family

Information regarding educational attainment, occupation, employment status and marital status of both parents was collected at baseline (See Appendix IX). This information was used to calculate the SES status of each parent and family using the Hollingshead Four Factor Index of Socioeconomic Status. In addition, the Hollingshead Index of Social Position

(ISP) was calculated for each family in order to assign the family to a social class category (Lantos, 2015).

4.5.3 Cardiac diagnosis and medical management information

Information regarding the type of CHD, presence of genetic and extracardiac abnormalities, HIV status (recorded as HIV positive, HIV negative or unknown), complications, medication use and risks factors for CHD was collected from the patient's medical record at baseline (See Appendix X).

The children's CHD was classified according to the nature of the defect as cyanotic or acyanotic (See Appendix I), and the medical severity of the cardiac disease was rated by a paediatric cardiologist using the Cardiologists Perception of Severity Scale (See Appendix II).

4.5.4 Cardiovascular status

Information regarding the children's cardiovascular status, including vital signs (heart rate, respiratory rate and blood pressure) was collected from the patient record. Non-invasive pulse oximetry was used to assess the percutaneous oxygen saturation (SpO_2) at baseline. A SpO_2 of less than 85% on room air was considered to be indicative of cyanosis (Brown, 2014; Kemper et al., 2011). This information was retrieved from the patient's medical record at baseline (See Appendix XI).

As vital signs and oxygen saturation (SpO_2) was not routinely taken at the cardiology clinic, cardiovascular status at three-month and six-months post-cardiac intervention was established on the grounds of the presence of cyanosis at baseline and the need for multiple cardiac surgeries to optimise cardiovascular function (CHD severity).

4.5.5 Surgical intervention and post-operative medical course information

Information regarding the child's surgery including age at first surgery, aim of the surgery (palliation, staged correction or correction), surgical access, CPB time and aorta cross-clamp time was collected from the child's medical record post-operatively.

In addition, information regarding the child's post-operative medical course, including the presence of seizures, the need for cardiopulmonary resuscitation, prolonged mechanical ventilation, peri-operative and post-operative complications, cardiac ICU length of stay, post-surgery hospital length of stay and total length of hospital stay was also collected from the patient's medical record (See Appendix X).

4.5.6 Anthropometric measurements

The scientific statement of AHA and AAP on the evaluation and management of children with CHD recommends that growth be carefully monitored. This includes weight, length/height and head circumference (Marino et al., 2012).

At baseline, length (height) and weight was routinely measured on admission to either the cardiothoracic ward or cardiology unit by the nursing personnel, and documented in the patient's file. At the three-month and six-month visits, length (height) and weight was routinely measured by the nursing personnel at the clinic and noted in the patient file and/or in the child's Road to Health Booklet (RTHB) (See Appendix XI).

Children were weighed using a digital baby scale and the measurement was noted in kilogram (kg) to a single decimal point. Length was determined by lying the child down on a firm surface. The child's legs were straightened, and a tape measure was run alongside the child stretching from the crown of the head to the heels. Length was measured in centimetre (cm). The same digital scale available in the cardiothoracic ward and the paediatric clinic respectively, and the same procedure for measuring the children's length, were used throughout the study.

Head circumference was not measured routinely by the nursing personnel and was measured by the researcher. A flexible non-stretchable measuring tape was used. The measuring tape was placed around the child's head at the broadest part of the head above the ears and midway between the eyebrows and the hairline to the occipital prominence at the back of the head. Head circumference was recorded in centimetres (cm).

The World Health Organization (WHO) child growth standards for length-for-age, weight-for-age and head circumference-for-age for girls and boys were used to determine z-scores for the anthropometric measurements (WHO, 2006). It is known that children with genetic abnormalities such as DS follow different growth trajectories from children without genetic abnormalities. Children with DS have lower birth weights and grow slower. DS is also characterised by short stature (Zemel et al., 2015). It is recommended that specific growth charts for special populations be used to evaluate growth outcomes in children with disorders that interfere with their growth, such as DS (CDC, 2016b; Zemel et al., 2015; Van Gameren-Oosterom et al., 2011; Myrelid et al., 2002). Zemel et al. (2015) recommends the use of the latest published DS-specific growth charts as growth in the contemporary population of children with DS has improved considerably due to medical advances. For this study, the latest DS-specific growth charts published in the US in 2015 were used to calculate z-scores for growth parameters of children with CHD with DS in the current study (Zemel et al., 2015). No DS-specific growth standards are currently available for SA.

4.5.7 Neurodevelopmental status

The BSID-III was used to determine developmental outcome. The motor, cognitive and language scales of the BSID-III were administered by a physiotherapist with extensive paediatric experience (Bayley, 2006b). Administration of the test followed the guidelines as outlined in the administration manual (Bayley, 2006a). Due to test security concerns, Person Inc. does not permit the appending of any assessment products to this thesis. All Pearson Inc. assessment products are copyright protected.

4.5.8 Neurological status

The AHA statement on the developmental assessment of young children with CHD recommends that a neurological assessment form part of the developmental assessment. This is to include the assessment of active and passive muscle tone and deep tendon reflexes (Marino et al., 2012).

Muscle tone, deep tendon reflexes, clonus and Babinski were assessed by the researcher as part of the neurological examination at baseline, and at the three-month and six-month post-cardiac intervention follow-up visits. The neurological examination was done with the child positioned in supine (See Appendix XI).

Muscle tone of the limbs was determined by moving the limb passively through the range of motion at different velocities whilst the resistance to movement was evaluated. Muscle tone was then classified as being increased, normal or decreased.

Deep tendon reflexes (biceps-, triceps-, patellar- and Achilles tendon) were tested using a reflex hammer. Tendon reflexes were classified as increased, normal or decreased. Babinski and clonus were also tested as part of the reflexes, and test findings were reported as either positive or negative.

4.5.9 Neurodevelopmental risk stratification

The risk of adverse developmental outcome was classified as low or high. Data was collected regarding risk factors as part of the medical and surgical data.

Children were deemed to be at high-risk of adverse neurodevelopmental outcome if they required surgery during infancy and if they had a cyanotic heart lesion. In addition, CHD with the following co-morbidities were considered to be at high-risk: prematurity, genetic syndromes associated with developmental difficulties, cardiopulmonary resuscitation at any point, prolonged hospitalisation post-surgery (> two weeks); peri-operative seizures, mechanical ventilation prior to cardiac surgery, significant neuroimaging abnormalities

and/or the presence of microcephaly (Marino et al., 2012). These variables (or risk factors) were also investigated for their association with developmental outcome (See Appendix X).

4.5.10 Health-related quality of life

The PedsQL™ was used to determine parents' perception of the impact of CHD and its treatment on their child's function and ability to derive satisfaction in various aspects of life, including physical, psychological and social domains. It is a multidimensional measure that is brief and easy to administer.

As children 36 months and younger were included in this study the PedsQL™ Infant Scales (1-24 months) and PedsQL™ 3.0 Cardiac Module for toddlers (2-4 years) were used. As young children were included in the study, parents served as proxy-raters and completed the questionnaires (Raat et al., 2006; Goldbeck and Melches, 2005). Due to test security concerns, Mapi Research Trust does not permit the appending of their assessment products to this thesis. All Mapi Research Trust assessment products are copyright protected.

4.5.11 Parenting stress

The PSI-SF was used to measure the levels of stress experienced by parents parenting a child with CHD. Parenting stress levels also served as a proxy for the burden of care. Due to test security concerns, Psychological Assessment Resources, Inc. (PAR) does not permit the appending of their assessment products to this thesis. All PSI-SF assessment products are copyright protected.

4.5.12 Burden of Care

Burden of care served to determine the impact of a child's illness on family life. Information regarding the burden of care was included in the family information data sheet at baseline, and the family burden of care data sheet at three-month and six-month post-cardiac intervention (See Appendix IX and Appendix XII).

Data items relating to burden of care were adapted from the PedsQL™ Family Information Form developed by (Varni et al., 2007). Items on which data was collected included the number of times the child was hospitalised and the reasons for the hospitalisation (data was collected regarding admissions before cardiac surgery and between follow-up visits), the number of days the child was too ill to play or get up, and the number of days the child required special care as a result of his/her physical health. If the parent worked outside of the home, information was gathered on the number of days the parent missed work due to their child's ill health, how often their child's physical health affected their daily routine at work and how often their child's physical health affected their ability to concentrate at work.

4.6 Procedure for Phase I and Phase II

Phase I

The list of children scheduled for admission for cardiac surgery each week was e-mailed to the researcher by the Cardiothoracic Surgery Department on the Friday before, so that the researcher could review the surgery list to identify potential study participants. The researcher visited the cardiothoracic ward each Monday at midday to establish which children had been admitted, and to identify those who met the inclusion criteria for the study based on the information in their medical record. Then the updated surgery list for the week was reviewed to identify children going in for surgery either on a Tuesday, Wednesday or Thursday morning so that recruitment could be prioritised, and children who were included could be assessed before going in for surgery. This strategy was aimed at maximising the number of participants included in this study. The only feasible opportunity to do the baseline assessment was on the day of admission, which in most cases was the day before the child was scheduled to undergo cardiac surgery.

Parents of children who met the inclusion criteria were approached in the cardiothoracic ward by the researcher after admission. The researcher informed the parents about the research study and invited them to participate. Parents who showed interested in participating were given an information letter, which was available in English, Afrikaans or Sesotho. Parents were provided with an opportunity to read through the document in their language of choice and ask questions. A translator was available, if needed.

Once written informed consent had been obtained from the parents, as well as written permission for their child's participation, the family was included in the study sample. Upon inclusion in the study, the researcher gathered information regarding the nature and severity of the CHD and medical management of the child's heart disease from the medical record and/or through consultation with the attending paediatric cardiologist.

Baseline

The child's vital signs (heart rate, respiratory rate, and blood pressure), oxygen saturation, weight and height/length, as measured by the nursing personnel in the cardiothoracic ward on admission, was sourced from the child's medical record and recorded. The child's head circumference was measured by the researcher and recorded.

The assessment took place in a doctor's consultation office in the cardiothoracic ward to ensure privacy and a quiet environment with minimal distractions. The assessment started with the physical assessment of the child to ensure that all physical tests were completed before the child went in for surgery.

The researcher administered the BSID-III. The test was administered with the child seated on the parent's lap at a table or in the case of older children, it was performed with the child seated on a child-sized chair at a child-sized table. A therapy mat was available for testing of activities such as rolling and crawling, where age appropriate. The mental scale was administered before the motor scale, as recommended in the BSID III administration manual. Testing started at the child's chronological age or where indicated at the child's corrected age for the cognitive, language and motor scales (Bayley, 2006b).

Following the administration of the BSID III the researcher performed a neurological examination with the child positioned in supine on an examination table or on a therapy mat. The neurological examination included the testing of muscle tone, deep tendon reflexes, Babinski and clonus.

Following the physical examination the researcher provided the parents with feedback on the child's developmental performance on the BSID-III, identifying areas of strength and

weakness. In cases where there were developmental concerns, it was discussed with parents.

The researcher interviewed the parents to gather demographic and socioeconomic information, as well as information regarding their current burden of care. The parents then completed two brief standardised questionnaires, the PedsQL™ which is a parent-proxy rated questionnaire that serves to measure parents' perception of their child's HRQOL, followed by the PSI-SF which serves to measure the levels of parenting stress. The questionnaires were available in English, Afrikaans and Sesotho. The researcher and a translator, if necessary, were present to answer any questions during the completion of the questionnaires.

All children participating in the study then underwent cardiac intervention in the form of either cardiac surgery or percutaneous cardiac catheterisation. All parents were informed on assessment that they would be followed-up as part of the study at their routine post-cardiac intervention cardiology follow-up appointment.

Phase II

Three-month post cardiac intervention follow-up visit

Upon discharge, the researcher established the child's paediatric cardiology clinic follow-up date as booked by the cardiothoracic ward nursing. This appointment was scheduled at three-month post-cardiac intervention. The appointment date was then confirmed telephonically with the paediatric cardiology clinic by the researcher.

Following discharge the researcher contacted the cardiothoracic department to retrieve the child's surgical and post-operative medical course information from the child's medical record. In cases of percutaneous cardiac catheterisation the cardiology department was contacted for procedure related information (See Appendix X on medical and peri-operative and post-operative information).

The researcher contacted parents telephonically and via Short Message Service (SMS) text message to remind them of their scheduled three-month study follow-up visit the week before and on the day before the scheduled appointment. Parents were accompanied from the cardiology clinic to the Physiotherapy Department for the three-month assessment.

Nursing personnel at the paediatric cardiology clinic measured the weight and height/ length of the child. The values were retrieved from the clinic file or RTHB, and recorded by the researcher when the child was collected from the clinic. The child's head circumference was measured by the researcher.

All the measures done at baseline were repeated, namely the BSID-III, neurological assessment, interview regarding burden of care and the completion of the two standardised questionnaires, the PedsQL^{TM} and PSI-SF. The same testing, interview and questionnaire procedures were followed, as described at baseline.

Following the physical examination the researcher provided the parents with feedback on the child's developmental performance on the BSID-III. Areas of strength and concern were highlighted. In cases where children were found to be developmentally at risk or presented with developmental delays based on their developmental performance on the BSID-III, parents were provided with suitable advice regarding developmental stimulation in line with the developmental items tested on the BSID-III. Children with developmental concern**s** were also referred to the indicated EI services (PT, OT and ST) at their nearest service point, if they were not already accessing services. Parents were also provided with feedback regarding their levels of parenting stress and their perception of their child's HRQOL in relation to baseline scores.

At the end of the follow-up visit, an appointment was made for their six-month post-cardiac intervention study follow-up. Where possible the researcher tried to combine the follow-up visit with other scheduled appointments at the hospital to decrease the burden placed on parents.

Six-month post-cardiac intervention follow-up visit

The researcher contacted parents telephonically and via SMS text message to remind them of their scheduled six-month study follow-up visit the week before and the day before the scheduled appointment. The six-month follow-up again took place at the Physiotherapy Department, Universitas Academic Hospital. This was a venue already familiar to parents.

Nursing personnel at the paediatric cardiology clinic or the child's local clinic measured the weight and height/ length. The values were retrieved and captured by the researcher during the visit. The child's head circumference was measured by the researcher.

The same measures were repeated as done at baseline and at the three-month follow-up, namely the BSID-III, neurological assessment, interview regarding burden of care and the completion of the two standardised questionnaires, the PedsQL^{TM} and PSI-SF. The same testing, interview and questionnaire procedures were followed as described for baseline and the three-month follow-up.

Following the physical examination, the researcher provided the parents with feedback on the child's performance on the BSID-III. Areas of strength and concern were highlighted. In cases where children were found to be developmentally at risk or presented with developmental delays based on their developmental performance on the BSID-III, parents were provided with suitable advice regarding developmental stimulation in line with the developmental items tested on the BSID-III. Children with developmental concern**s** were also referred to the indicated EI services (PT, OT and ST) at their nearest service point, if they were not already accessing services. Parents were also provided with feedback regarding their levels of parenting stress and their perception of their child's HRQOL in relation to their baseline and three-month follow-up visit scores.

Progress through Phase I and II of the study was monitored and data regarding mortality, loss to follow-up and non-compliance was captured (See Appendix XIII). Figure 4.2 below provides a flow diagram depicting the study procedure.

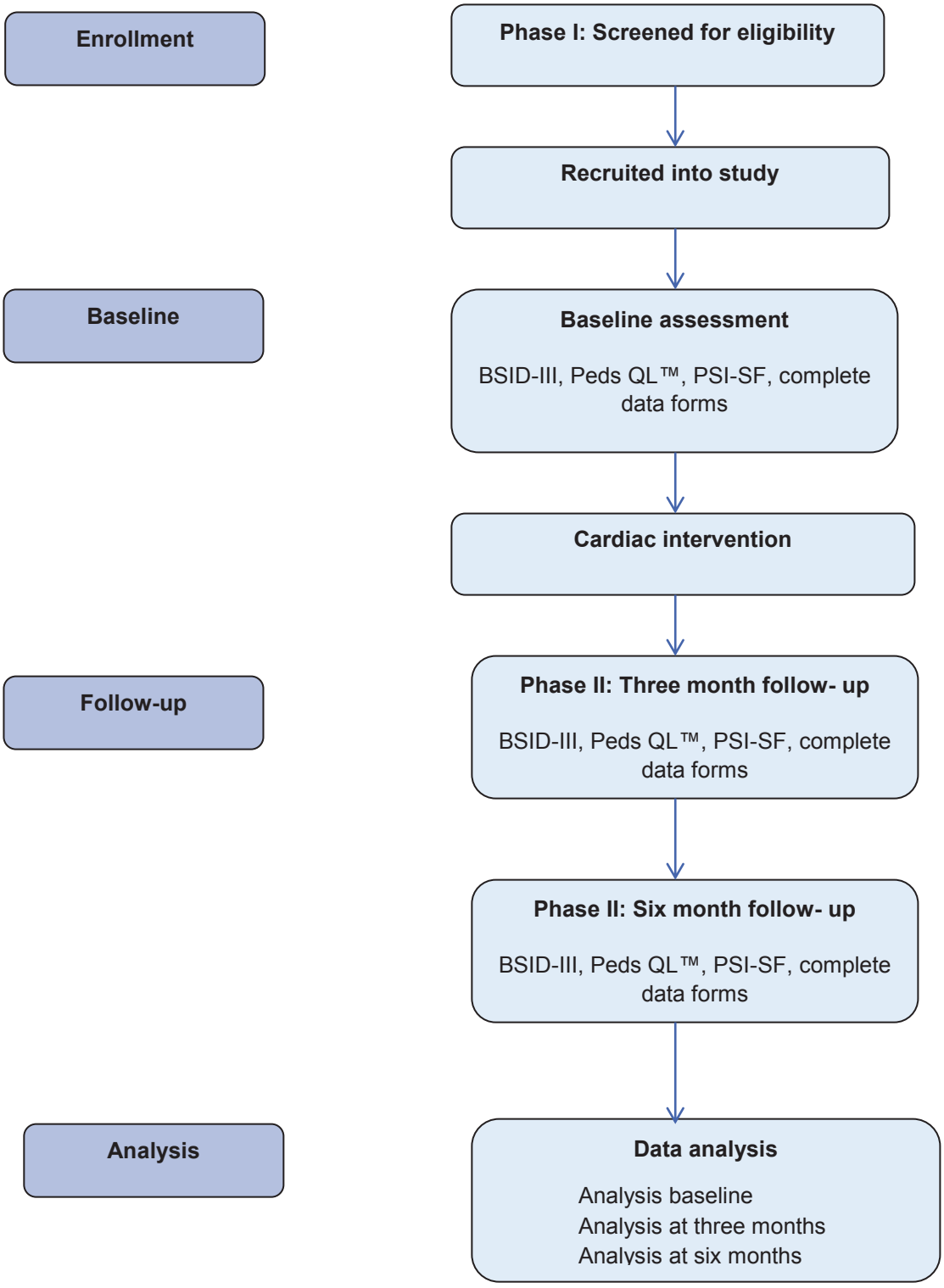

Figure 4.2 Flow diagram of the study procedure

4.7 Measures to limit attrition

Most of the children and their families treated at the cardiology unit at Universitas Academic Hospital are public sector patients, and families often come from poor socioeconomic circumstances. The majority of children and their families rely on inter-hospital or public transport to access cardiology services. Attendance of follow-up cardiology appointments in many cases is irregular and up to 45% of children do not attend their scheduled follow-up appointments (Brown, 2016).

In order to reduce loss to follow-up, inconvenience and the financial burden on families, follow-up appointments were scheduled on the same dates that the children had their scheduled cardiology clinic follow-up visits.

At baseline, a contact number was taken for the primary caregiver, which in most cases was the mother. Where there was an alternative contact number for an additional family member it was taken as well. The number of the primary caregiver was phoned in order to confirm that it was a valid number. Parents were contacted telephonically and via SMS text message one week before the scheduled study follow-up and the day before to remind them of the scheduled appointment. Studies by Leong et al. (2006), Downer et al. (2006) and Car et al. (2012) found that SMS text message reminders improved attendance of healthcare appointments. No confidential information was shared via SMS text message, only the date and time of the study follow-up.

If children failed to arrive for scheduled follow-up appointments, the parents were contacted on the same day, and the appointments were rescheduled at the earliest possible convenience.

A contribution was also made toward the travelling costs of participants to encourage the attendance of follow-up visits.

4.8 Statistical analysis

A sample size of 40 children and their parents had a 90% power to detect a difference in means of 10 based on a standard deviation of 15, taking into account a possible 15% loss to follow-up and a 10% non-compliance based on the BSID III, as the main outcome measure.

The data were not subjected to a test of normality as the sample size was not large enough for a proper test of normality. The assumption was that the data followed a normal distribution.

Sample characteristics and clinical variables were presented as means with standard deviations and medians with ranges for continuous data and frequencies with percentages for categorical data.

In addition to being treated as a numerical score, developmental outcomes within each developmental domain in the BSID-III (cognitive, language, and motor), growth parameters and parenting stress levels were classified at each assessment in accordance with each measure-specific classification system. Classification data was reported using frequencies with percentages.

Within group changes over time, from baseline to both three-month and six-month post-cardiac intervention, for growth parameters (length, height and head circumference), BSID-III domain scores (cognitive, language and motor), neurological status, PedsQL™ total scores and PSI-SF total scores were calculated using a 95% confidence intervals on the difference between z-score means. Testing was done at the 0.05 level of significance.

A paired T-test was used to assess difference between means of groups at baseline as part of the attrition analysis. Statistical significance was determined at a p-value of less than 0.05.

The association between identified variables and specific outcomes, including the BSID-III scores for each domain (cognitive, language and motor), PedsQL™ total score and PSI-SF

total scores at baseline, and three-months and six months post-cardiac intervention, was determined using analysis of variance (ANOVA). Mean values for variables significantly associated with key outcomes over time were analysed to determine upward or downward trends in associations. In addition, a regression analysis was done to determine variables that were predictive of neurodevelopmental, HRQOL and parenting stress outcomes using ANOVAs. A linear regression model was used for each of the key outcome namely neurodevelopment (cognitive, motor and language), HRQOL and parenting stress. The effects used were the subcategories under each outcome. Interaction effects were also tested where appropriate. The code for the ANOVA models used are presented in Appendix XIV.

All data was entered into EXCEL spreadsheets. Descriptive statistics were calculated in EXCEL, while advanced statistical analysis was performed using R-Software in consultation with a Biostatistician.

The results of this study are presented in Chapter five.

CHAPTER 5

RESULTS OF PHASE I AND PHASE II

The results for Phase I and II of this study will be presented in this chapter and will be briefly commented on. Study attrition will be outlined, and the reasons for attrition will be explained.

Growth, neurodevelopmental, HRQOL, burden of care and parenting stress outcomes will be presented prior to cardiac surgery, and at three-month and six-month post-cardiac intervention. In addition, outcomes for neurodevelopment, HRQOL and parenting stress will be compared over time. The indication for early developmental intervention services will be established based on developmental performance on the BSID-III. Neurodevelopmental outcomes will further be used in the development of an appropriate home-based, parent-driven developmental stimulation programme presented in Chapter seven.

Variables associated with neurodevelopmental and HRQOL outcomes, as well as those variables associated with levels of parenting stress will be identified and briefly described.

The purpose of routine cardiac neurodevelopmental follow-up is to cater for the entire spectrum of children presenting with CHD. For this reason, children who were diagnosed with a genetic comorbidity were not excluded from this study. The outcome of participants with a genetic comorbidity and cyanotic heart defects were of special interest, and key findings for these subgroups will also be presented.

The findings and further implications of these findings will be discussed in depth in Chapter six.

5.1 Study attrition

Forty-eight participants were recruited into the current study. Eight participants were subsequently lost to inclusion. Forty children were enrolled into this study at baseline (Refer to Figure 5.1). The study attrition for this study is presented in Figure 5.1 (on the following page).

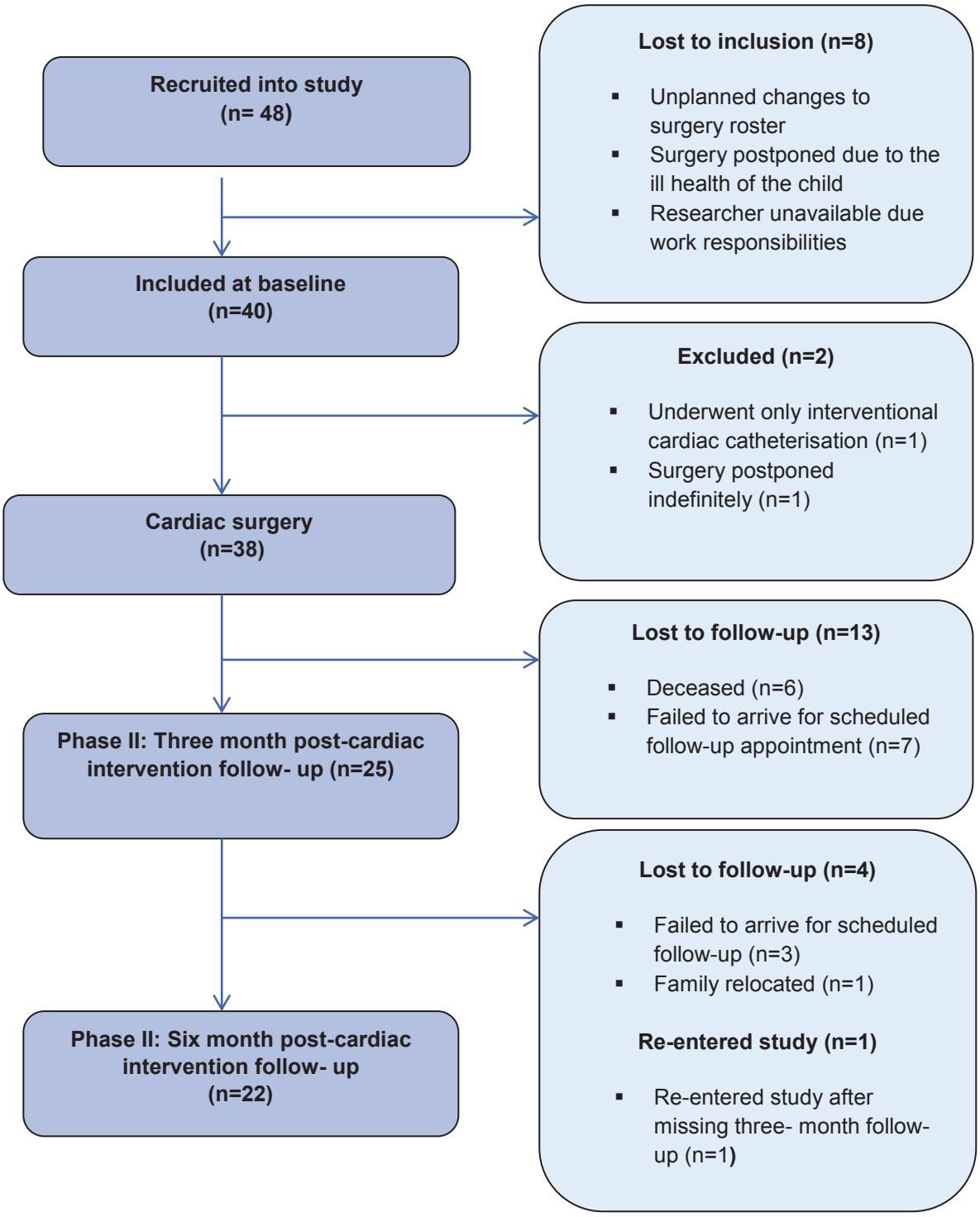

Figure 5.1 Loss to follow-up over the study

The mechanisms that were put in place to limit attrition in this study at the Paediatric Cardiology Unit, Universitas Academic Hospital in Bloemfontein were described in Chapter four (Refer to section 4.7).

Forty children were included in this study at baseline following a recruitment period of 17 months. Over the duration of the study, 19 participants were lost to follow-up, which equated to 47.5% of the sample being lost to follow-up at one or more point in time across this study.

The reasons for attrition are outlined below.

Excluded following baseline (n=2)

Two participants had to be excluded from this study following their baseline assessment as they failed to undergo cardiac surgery. One participant only underwent interventional cardiac catheterisation but no surgery, whilst the other participant's surgery was postponed indefinitely beyond the time frame of the current study due to the ill health of the child.

Mortality (n=6)

Six participants (15%) died following cardiac surgery. Three participants died in hospital following significant post-operative complications. Two participants died in the cardiothoracic ICU post-cardiac surgery after suffering a cardiac arrest and unsuccessful resuscitation. One participant survived a cardiac arrest but sustained a severe hypoxic brain injury, and died from respiratory-related complications following a three-month period of hospitalisation post-operatively.

All three children who died post-operatively in the cardiothoracic ICU underwent cardiac surgery during infancy. Child one underwent an AVSD repair and had an accompanying genetic comorbidity; the CHD was further complicated in this case by PHTN. Child two underwent a coarctation repair and was also born prematurely. Child three underwent a VSD repair and had an accompanying genetic comorbidity.

Three participants died at home within three-months of hospital discharge following their first cardiac surgery. The reasons for mortality as reported by the mothers in all three cases were respiratory-related complications.

Child one had undergone a VSD repair; the CHD was also complicated by PHTN. Child two had undergone a VSD repair and also had an accompanying genetic comorbidity. Child three had a DORV and AVSD and had undergone palliative surgery; the child also had an accompanying genetic comorbidity.

The majority of the participants (66.7%) who died post-operatively had an accompanying genetic comorbidity. In all cases the genetic comorbidity was DS. The children who died were aged between two and 17 months.

Non-compliance with scheduled follow-up visits (n=5)

Five primary caregivers could be contacted via telephone and SMS text message, but still failed to comply with their scheduled follow-up appointments despite repeated efforts to encourage attendance and rescheduling of missed appointments.

Three of the aforementioned primary caregivers and their children failed to arrive for both their three-month and six-month post-cardiac intervention follow-ups, whilst the other two caregivers and their children failed to arrive for only their six-month post-cardiac intervention follow-up.

Untraceable (n=4)

Three primary caregivers and their children were lost to both their three-month and six-month post-cardiac intervention follow-up as they were untraceable. Contact numbers provided by the primary caregivers at the time of their baseline assessments were either no longer in service, switched off or belonged to another person resulting in the caregivers not being able to be contacted or traced. These caregivers and their children were also lost to cardiology services at Universitas Academic Hospital.

One primary caregiver and her child missed their three-month follow-up as well as their cardiology follow-up and could not be contacted or traced. The caregiver and child unexpectedly re-appeared at cardiology services and the six-month follow-up assessment could be done, despite being later than scheduled. One caregiver and child were untraceable by the time of their scheduled six-month post-cardiac intervention follow-up. The contact number provided was no longer in service and they could not be traced.

Family relocation (n=1)

One primary caregiver and her child relocated to another province in SA, and were unable to attend their six-month post-cardiac intervention follow-up.

In the light of the high attrition rate, an attrition analysis was conducted for key variables at baseline for all the participants, those lost to follow-up, and those who remained in this study throughout. All participants were compared to those lost to follow-up and those remaining in the study, and those remaining in the study were compared to those lost to follow-up.

The attrition analysis is presented in Table 5.1 for child-related variables and in Table 5.2 for family-related variables. Any participant who missed one or more follow-up visit is represented in the lost to follow-up group, as were those who died and relocated. Values are reported as frequencies with percentages, medians with ranges, and means with standard deviations. P-values have been calculated for the difference between means between groups for relevant variables using paired T-tests.

Table 5.1 Attrition analysis for key child-related variables at baseline

Baseline characteristics: Child-related variables	All participants at baseline (n=40)	Participants lost to follow-up (n=19)	Participants remaining in study (n=21)	P-values all versus those lost	P-values all versus those remaining	P-values lost versus those remaining
Age baseline (months)						
Median	7.4	7.3	8.8			
Mean and SD	9.2 (± 5.4)	8.4 (± 5.1)	9.9 (± 5.7)	0.676	0.729	0.509
Gender						
Male	15 (37.5%)	7 (36%)	8 (38%)	0.960	0.960	0.963
Female	25 (62.5%)	12 (63.2%)	13 (61.9%)	0.960	0.960	0.963
Genetic comorbidity	10 (25%)	5 (26.3%)	5 (23.8%)	0.912	0.920	0.857
Disease severity	Moderate	Moderate	Moderate			
BSID composite cognitive score						
Median	85	85	95			
Mean and SD	84.9 (± 19.0)	82.6 (±19.6)	86.9 (±18.7)	0.681	0.691	0.487
BSID composite language score						
Median	91	91	91			
Mean and SD	90.5 (± 14.1)	88.5 (±13.7)	92.2 (±14.6)	0.621	0.657	0.418
BSID composite motor score						
Median	82	79	85			
Mean and SD	79.5 (± 17.5)	78.2 (±17.5)	80.7 (±17.8)	0.793	0.808	0.663
Weight-for-age Z-score						
Median	-3.1	-3.1	-2.3			
Mean and SD	-2.5 (±1.5)	-2.9 (±7.7)	-2.2 (±1.5)	0.330	0.367	0.10
Height-for-age z-score						
Median	-1.9	-2.2	-1.3			
Mean and SD	-2.2 (± 2.5)	-2.7 (±1.8)	-1.7 (±2.9)	0.553	0.223	0.591

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table 5.2 Attrition analysis for key family-related variables at baseline

Baseline characteristics Family-related variables	All participants (n=40)	Participants lost to follow-up (n=19)	Participants remaining in study (n=21)	P-values all versus those lost	P-values all versus those remaining	P-values lost versus those remaining
Age of mother (years)						
Median	30	32	30			
Mean and SD	29.6 (±8.04)	28.2 (±7.7)	30.9 (±8.3)	0.519	0.568	0.294
Maternal education	Grade 9-11	Grade 9-11	Grade 9-11			
Mothers unemployed	33 (83%)	18 (94.7%)	15 (71.4%)	0.201	0.317	0.052
SES	Lower class	Lower class	Lower class			
Parental stress						
Median	90	90	90			
Mean and SD	83.8 (± 19.2)	84.6 (±17.7)	83.1 (±20.8)	0.833	0.856	0.734
HRQOL						
Median	80.6	85	80.6			
Mean and SD	77.6 (± 12.4)	78.9 (±19.6)	76.5 (±10.9)	0.735	0.706	0.544
Distance to cardiac service (km)						
Median	162.6	185.1	180.2			
Mean and SD	202.8 (± 188.7)	162.4 (± 176.1)	218.7 (±202.3)	0.728	0.766	0.578

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

There were no statistically significant differences for child-related or family-related variables between all participants at baseline and those participants remaining in the study throughout. Significant attrition bias was therefore not introduced in this study, and the participants remaining in the study could be considered to be representative of all participants at baseline.

In addition, there were also no statistically significant differences for child-related and family-related variables between all participants at baseline and those lost to follow-up. Neither was there any statistically significant difference between participants remaining in this study throughout and those lost to follow-up. Therefore, no specific child-related or family-related

variables could be assigned to contribute significantly to loss to follow-up in this study.

5.2 Baseline sociodemographic information for all participants

5.2.1 Demographic information

Demographic information collected for all participants prior to cardiac intervention (baseline) is presented in Table 5.3 for child-related variables and in Table 5.4 for family-related variables. Relevant information was extracted from the family information data sheet that was completed at baseline. Values reported are frequencies with percentages, medians with ranges, and means with standard deviations.

Table 5.3 Demographic information of the child

Child-related variables	Study sample (n=40)
Age of child at baseline (months)	
Median (range)	7.4 [1.4 – 20.9]
Mean and SD	9.2 (± 5.4)
Gender	
Male	15 (37.5%)
Female	25 (62.5%)
Gestational age (weeks)	
Median (range)	38 [31 – 41]
Mean and SD	37.5 (±2.0)
Birth weight (grams)	
Median (range)	2800 [1640 – 3950]
Mean and SD	2878.5 (±608.3)
Ethnicity of the child	
Black African	30 (75%)
Mixed race	9 (22.5%)
White	1 (2.5%)

The majority of the participants in this study were of black African ethnicity, which is representative of the ethnic profile of the South African population. Although the median gestation age at birth for all participants was 38 weeks, nine participants (22.5%) were born preterm (< 37 weeks gestation) with a gestational age ranging from 31 to 36 weeks. Thirty participants (75%) had a birth weight within the normal range (2500- 4000 grams). Of these children categorised as having a normal birthweight, 23 (76.7%) had a birth weight under 3000 grams. Therefore, despite the majority of the participants having been classified as

having a normal birth weight, most tended to have a birth weight on the lower side of the normal range.

Table 5.4 Demographic information of the family

Family-related variables	Study sample (n=40)
Primary caregiver	
Mother	39 (97.5%)
Father	1 (2.5%)
Age of the mother (years)	
Median (range)	30 [16 – 43]
Mean and SD	29.6 (±8.0)
Number of siblings	
Median (range)	1 [0 – 4]
Mean and SD	1.2 (±1.1)

Mothers were the primary caregiver in all but one instance, where the father fulfilled the role due to the mother's mental health challenges. The age of the mothers varied considerably. Of the mothers, 15% were younger than 21 years, while 32.5% were 35 years or older.

5.2.2 Socioeconomic status

SES was reflected by the parents' level of education, occupational prestige and employment status. The Hollingshead Index of Social Position was calculated to reflect the SES of each family.

Most fathers were not present at the baseline assessment, and mothers were asked to report on the education level, occupation and employment status of the child's father.

The SES for all participants is presented in Table 5.5 (See table on the following page). Values reported are frequencies with percentages.

Table 5.5 Socioeconomic status of the families

Variable	Study sample (n=40)
Level of education of mothers	
University graduate	1 (2.5%)
Partial university or specialised training	5 (12.5%)
High school graduate	10 (25%)
Grade 9-11	18 (45%)
Grade 7-8	5 (12.5%)
Grade 6 or less	1 (2.5%)
Employment status of mothers	
Unemployed	33 (82.5%)
Part-time employment	2 (5%)
Full-time employment	5 (12.5%)
Level of education of fathers	
University graduate	1 (2.5%)
Partial university or specialised training	3 (7.5%)
High school graduate	13 (32.5%)
Grade 9-11	13 (32.5%)
Grade 7-8	4 (10%)
Unknown	6 (15%)
Employment status of fathers	
Unemployed	13 (32.5%)
Part-time employment	6 (15%)
Full-time employment	21 (52.5%)
Socioeconomic status of the family	
Lower class	35 (87.5%)
Lower-middle class	2 (5%)
Middle class	2 (5%)
Middle-upper class	1 (2.5%)

The average level of education for both mothers and fathers was grade nine to 11 (median and mean values were determined to be the same). Of the 33 mothers who were unemployed, 29 mothers (87.9%) stayed at home in order to care for their child, or as a direct result of unemployment. The other four mothers (12.1%) were still learners or college students at the time of this study.

The unemployment rate amongst fathers was high at 32.5%. Families in these cases tended to have no other source of income apart from child support grants provided by the government. More than half of the fathers (52.5%) were unskilled and worked as labourers or performed menial jobs. The majority of the families were from a low socioeconomic class.

5.3 Cardiac diagnostic and medical management information

The majority of the participants in this study resided in the Free State province (57.5%), with a large number of participants residing in the bordering Northern Cape Province (30%) of SA (Refer to Figure 4.1 under section 4.1 for a geographical representation of the provinces in SA).

The catchment area for participants in this study covered a wide geographical area of SA. The distance travelled by families to access cardiac services at the Paediatric Cardiology Unit at Universitas Academic Hospital in Bloemfontein is shown in Table 5.6. Values reported are frequencies with percentages, medians with ranges and means with standard deviations.

Table 5.6 Distance travelled to the cardiac service point

Variable	All participants (n=40)
Distance to cardiac service point (km)	
Median (range)	162.4 [12 – 782.8]
Mean and SD	202.8 (±188.7)
Distance to service point per category	
< 15 km	10 (25%)
Between 15 and 50 km	0 (0%)
Between 50 and 100 km	4 (10%)
>100 km	26 (65%)

The majority of the participants (65%) had to a travel a distance of over 100 kilometres to access cardiology services at the Universitas Academic Hospital in Bloemfontein. The majority of these families were dependent on the inter-hospital transport services provided by the RSA-DoH to commute to the cardiac centre. Only ten participants (25%) resided in Bloemfontein, where the cardiology service is located.

A paediatric cardiologist was involved in the care of all participating children prior to cardiac intervention. The participants' heart defects were classified according to the presence or absence of cyanosis. The majority of the participants (80%) in this study presented with acyanotic heart disease. The distribution of the study sample according to the type of congenital heart disease, based on the presence or absence of cyanosis is presented in Figure 5.2.

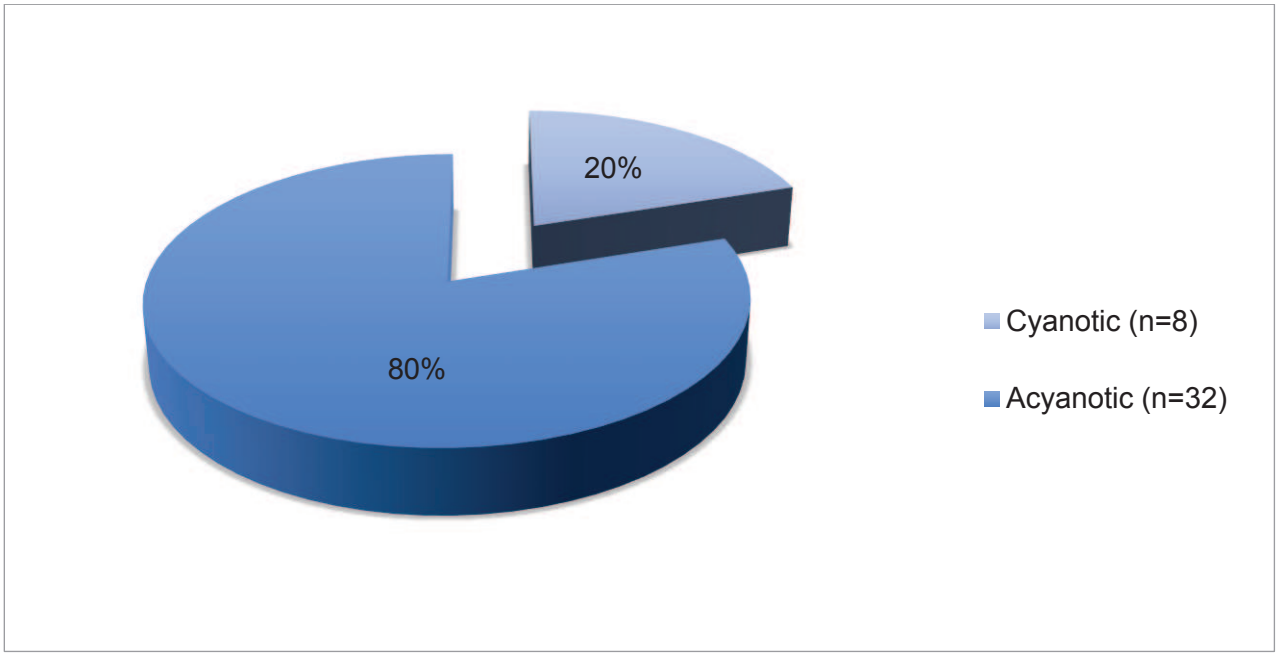

Figure 5.2 Classification of the type of congenital heart disease based on the presence of cyanosis (n=40)

The primary cardiac diagnosis and CHD classification was sourced from the participants' medical record and is presented in Table 5.7 (See table on the following page). Values reported are frequencies with percentages.

Table 5.7 Cardiac diagnosis and congenital heart disease classification

Variable	Study sample (n=40)
Primary cardiac diagnosis	
Acyanotic defects (n=32)	
VSD	15 (37.5%)
AVSD	9 (22.5%)
PDA	4 (10%)
Coarctation of the aorta	3 (7.5%)
Aortic stenosis	1 (2.5%)
Cyanotic defects (n=8)	
DORV	3 (7.5%)
TGA	1 (2.5%)
TAPVD	1 (2.5%)
HLHS	1 (2.5%)
Tetralogy of Fallot	1 (2.5%)
Tricuspid atresia	1 (2.5%)
Severity of the cardiac disease	
Mild	1 (2.5%)
Moderate	30 (75%)
Moderate to severe	8 (20%)
Severe	1 (2.5%)
Mean severity across all participants	**Moderate**
Complicated CHD	
Uncomplicated	12 (30%)
Complicated by PHTN and/ or CCF	28 (70%)

In the majority of cases, the cardiac disease was moderate in severity. The most commonly diagnosed congenital heart defects in this study sample were VSDs, followed by AVSDs.

Of the 28 participants who presented with complicated CHD, six participants (21.4%) presented with PHTN, 17 participants (60.7%) with CCF, and five participants (17.9%) with both PHTN and CCF.

Eighty-five percent of the participants were on prescription medications for their cardiac condition.

Relevant medical information was also collected from the participants' medical records and is presented in Table 5.8. Values reported are frequencies with percentages.

Table 5.8 Medical information of importance

Variable	Study sample (n=40)
Presence of a diagnosed genetic comorbidity	
No	30 (75%)
Yes	10 (25%)
Presence of extracardiac congenital abnormality	
No	37 (92.5%)
Yes	3 (7.5%)
HIV status of the child	
HIV negative	28 (70%)
HIV positive	0 (0%)
HIV status unknown	12 (30%)
Presence of known teratogens	
None	36 (90%)
Maternal Diabetes Mellitus	3 (7.5%)
Maternal hypertension	1 (2.5%)

Twenty-five percent of the participants were diagnosed with a genetic comorbidity; in all cases, the diagnosed genetic abnormality was DS.

Four participants presented with extracardiac congenital abnormalities, two with musculoskeletal abnormalities, one with duodenal atresia and one with an umbilical hernia.

No participants had tested HIV-positive at the time of their inclusion in this study. The HIV-status of 30% of the participants was unknown.

Concerning cardiovascular status, 20% of the children were diagnosed with cyanotic heart defects and presented with cyanosis prior to cardiac intervention. Cyanosis was defined as a percutaneous oxygen saturation (SpO_2) reading below 85%. Most of the children (87.5%) presenting with cyanosis before cardiac intervention, underwent either palliation or surgical procedures that would require further surgeries going forward to optimise their cardiovascular function.

5.4 Surgical intervention and post-operative medical course

Thirty-eight participants underwent cardiac surgery following their baseline assessment. The vast majority of these surgeries were elective in nature, and it was the first cardiac surgery for all the participants.

Relevant information pertaining to the cardiac surgery was extracted from the participants' surgical records and is presented in Table 5.9. Values reported are frequencies with percentages, medians with ranges, and means with standard deviations.

Table 5.9 Information pertaining to the cardiac surgery

Variable	Study sample (n=38)
Age at first cardiac surgery (months)	
Median (range)	7.5 [1.4 – 20.9]
Mean and SD	9.4 (±5.5)
Aim of the surgery	
Correction	28 (73.6%)
Staged correction	5 (13.2%)
Palliation	5 (13.2%)
Surgical access	
Median sternotomy	31 (81.6%)
Lateral thoracotomy	7 (18.4%)
Cardiopulmonary bypass time (min)	
Median (range)	104 [41 – 300]
Mean and SD	111.8 (±54.8)
Aorta cross-clamp time (min)	
Median (range)	76 [15 – 132]
Mean and SD	70.3 (±35.4)

The majority of the participants (68.4%) underwent their first cardiac surgery during infancy (< 12 months of age). However, the age at the time of first cardiac surgery ranged from 1.4 month to 20.9 months.

The majority of the participants underwent open-heart surgery with 68.4% of participants being placed on CPB during surgery. Twenty-seven participants (71%) had their aortas cross-clamped during surgery. CPB was done under relative hypothermia using cardioplegia

as the cardiac protection method.

Information pertaining to the participants' post-operative medical course following cardiac surgery was extracted from the participants' medical records. This included information on peri-operative and post-operative complications, cardiothoracic ICU length of stay, hospital length of stay post-surgery and total hospital length of stay. Information on the medical course post-cardiac surgery is presented in Table 5.10 (See table on the following page). Values reported are frequencies with percentages, medians with ranges, and means with standard deviations.

Table 5.10 Medical course following surgery

Variable	Study sample (n=38)
Peri-operative complications	
Yes	4 (10.5%)
No	34 (89.5%)
Cardiothoracic ICU length of stay (days)	
Median (range)	6 [3 – 28]
Mean and SD	7.5 (±5.6)
Post-operative complications	
Yes	7 (18.4%)
No	31 (81.6%)
Post-surgery hospital length of stay (days)	
Median (range)	9 [3 – 108]
Mean and SD	14.7 (±18.8)
Total hospital length of stay (days)	
Median (range)	11 [7 – 108]
Mean and SD	19.8 (±21.0)

The majority of participants had an uncomplicated post-operative medical course. However, five participants (13.2%) were mechanically ventilated for longer than seven days, and 12 participants (31.6%) had a cardiothoracic ICU length of stay extending beyond seven days.

Peri-operative complications occurred in four participants, three participants suffered a cardiac arrest and one participant presented with severe haemodynamic instability in the immediate post-operative period.

Post-operative complications in the cardiothoracic ICU occurred in seven participants. Complications included respiratory infections (n=6), a hypoxic brain injury (n=1) and wound sepsis (n=1).

Fifteen participants (39.5%) had a total hospital length of stay from the day of admission exceeding two weeks, while only eight participants (21.1%) had a total hospital length of stay exceeding two weeks from the day of surgery. The total hospital length of stay from admission is not always considered to be an accurate reflection of a complicated medical course in the current study setting. Many participants are admitted to hospital, and remain in hospital for extended periods prior to cardiac surgery due to surgeries being postponed or cancelled due to the illness of the child. The children are often kept in hospital rather than being discharged home for a short period, only having to return to hospital at great financial cost to the families. Keeping the children in hospital also curtails the risk of children not returning for rescheduled surgeries.

5.5 Growth outcomes

The WHO (2006) child growth standards and DS-specific growth charts (published in the US in 2015 by Zemel and colleagues) were used to determine z-scores for anthropometric measurements of children without and those with DS respectively.

Anthropometric data is presented as z-scores for weight-for-age, height-for-age and head circumference-for-age at baseline, and for three-month and six-month post-cardiac intervention in Table 5.11. Values are reported as medians and means with standard deviations.

Table 5.11 Anthropometric data

Variable	Baseline (n=40)	Three-months post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Weight-for-age z-score			
Median	-2.6	-2.1	-1.5
Mean and SD	-2.5 (±1.5)	-1.8 (±1,7)	-1.5 (±1.8)
Height-for-age z-score			
Median	-1.9	-0.8	-1.6
Mean and SD	-2.2 (±2.5)	-1.3 (± 1.8)	-1.8 (±1.6)
Head circumference-for-age z-score			
Median	-1.4	-1.0	-0.4
Mean and SD	-1.3 (±1.5)	-0.9 (±1.7)	-0.4 (±1.8)

Z-scores for participants were used to identify malnutrition, stunting and microcephaly in participants. The WHO Global Database on Growth and Malnutrition uses a z-score cut off point of less than -2 standard deviations (SD) to classify low weight-for-age and height-for-age as moderate malnutrition and stunting respectively, and z-scores of less than -3 SD as severe malnutrition and stunting respectively. A z-score cut-off point of less than -2 SD for head circumference-for-age is considered indicative of microcephaly.

The classification of growth status according to the WHO z-score classification guidelines indicating suboptimal growth (characterised by a z-score of <-2) for weight-for-age, height-for-age and head circumference-for-age is presented in Table 5.12. Values reported are frequencies with percentages.

Table 5.12 Participants with malnutrition, stunting and microcephaly

Variable	Baseline (n=40)	Three-months post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Malnutrition	27 (68%)	14 (56%)	9 (40.9%)
Stunting	18 (45%)	9 (36%)	8 (36.4%)
Microcephaly	10 (25%)	5 (20%)	3 (13.6%)

The majority (68%) of the participants presented with malnutrition prior to cardiac intervention, and of these participants with malnutrition 42.5% had severe malnutrition (z-score <-3 SD). A large number of participants (45%) also presented with stunting prior to cardiac intervention indicating that growth failure was more chronic in nature. There was a high incidence of microcephaly (z-score <-3 SD) with up to a quarter of participants presenting with microcephaly (z-score < -2 SD).

It is evident that growth was suboptimal in participants prior to cardiac intervention. The mean z-scores for all three growth parameters (weight, height and head circumference) at all three time points of assessment are presented graphically in Figure 5.3 for descriptive purposes.

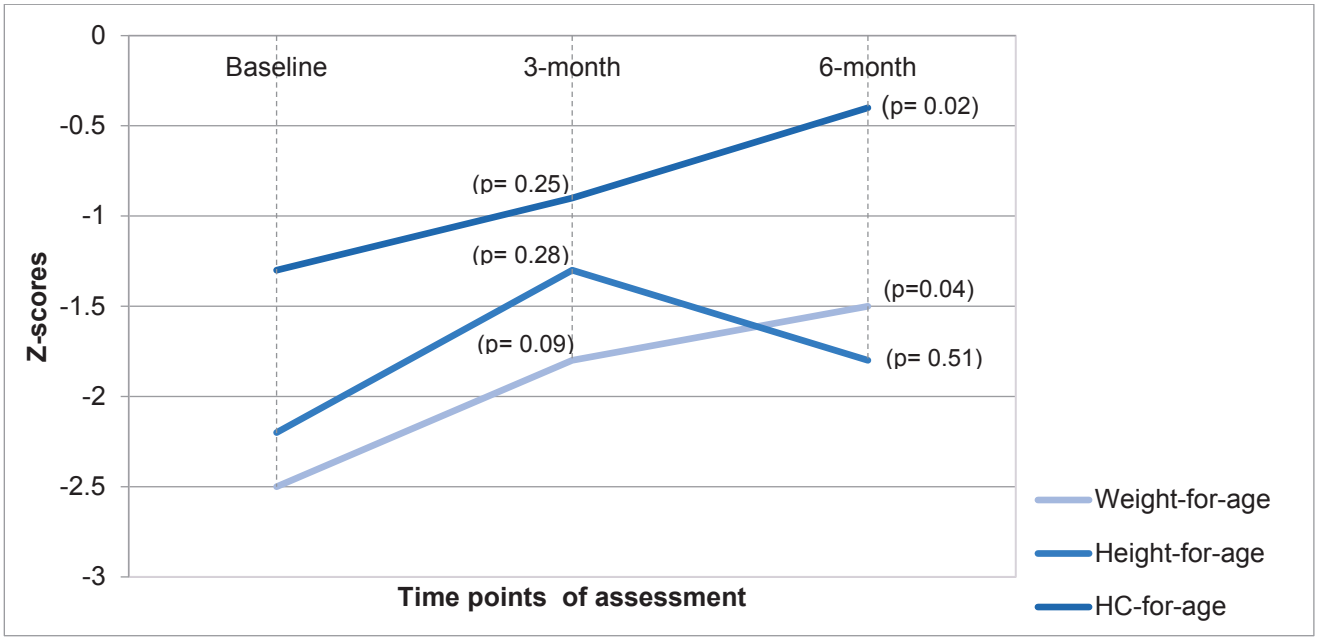

Figure 5.3 Mean z-scores for growth parameters over the study

Growth status across all growth parameters improved from before cardiac intervention to post-cardiac intervention, where at three-month and six-month post-cardiac intervention the mean z-scores for all parameters fell within the acceptable range (z-score > -2). The significance of the change in growth outcomes for all growth parameters over time is formally presented and commented on under 5.12.

Complete catch-up growth however had not occurred by six-month post-cardiac intervention, as the mean and z-scores were still below the 50th percentile (Z-score of zero) across all growth parameters. Seven participants (31.8%) still presented with severe malnutrition at six-month post-cardiac intervention.

Caregivers reported feeding difficulties in a quarter of the participants. Feeding difficulties reported included children struggling to suck, swallow and breathe during feeds due to respiratory distress, children tiring when feeding and GORD. Formal assessment of feeding skills however did not fall within the scope of this study.

5.6 Neurodevelopmental outcomes

Neurodevelopment status was assessed at three time points across this study. These assessments took place at baseline (prior to cardiac intervention), and at three-month and six-month post-cardiac intervention respectively. The age of the participants at the three assessment time points is depicted in Table 5.13. Values reported are medians with ranges and means with standard deviations.

Table 5.13 Age at neurodevelopmental assessment

Variable	Baseline (n=40)	Three-months post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Age at assessment (months)			
Median (range)	7.4 [1.4 – 20.9]	11.8 [4.6 – 25.5]	15 [7.4 – 30.4]
Mean and SD	9.2 (±5.4)	13.5 (±5.9)	16.7 (±6.4)

Age corrected neurodevelopmental outcomes will be presented as composite scores for the three subscales of the BSID-III, namely the cognitive, language and motor subscale. The developmental status of the participants at baseline, and at three-month and six-month post-cardiac intervention are presented in Table 5.14. Values reported are medians with ranges and means with standard deviations. The mean score on all three subscales of the BSID-III is 100.

Table 5.14 Cognitive, language and motor outcomes on the BSID-III

BSID-III subscale	Baseline (n=40)	Three-month follow-up (n=25)	Six-month follow-up (n=22)
Cognitive subscale			
Median (range)	85 [55 – 130]	90 [55 – 105]	90 [55 – 110]
Mean and SD	84.9 (± 19.03)	84.6 (±17.1)	83.4 (±18.3)
Language subscale			
Median (range)	91 [62 – 115]	89 [50 – 112]	81.5 [59 - 109]
Mean and SD	90.5 (±14.1)	88.4 (±15.9)	83.4 (± 15.5)
Motor subscale			
Median (range)	82 [46 - 112]	88 [46 - 112]	89.5 [49 - 121]
Mean and SD	79.5 (±17.5)	82.4 (± 19.8)	84.3 (±22.5)

For descriptive purposes, the mean composite BSID-III scores for all of the BSID-III subscales (cognitive, language and motor) at all three time points of assessment are presented graphically in Figure 5.4 for descriptive purposes.

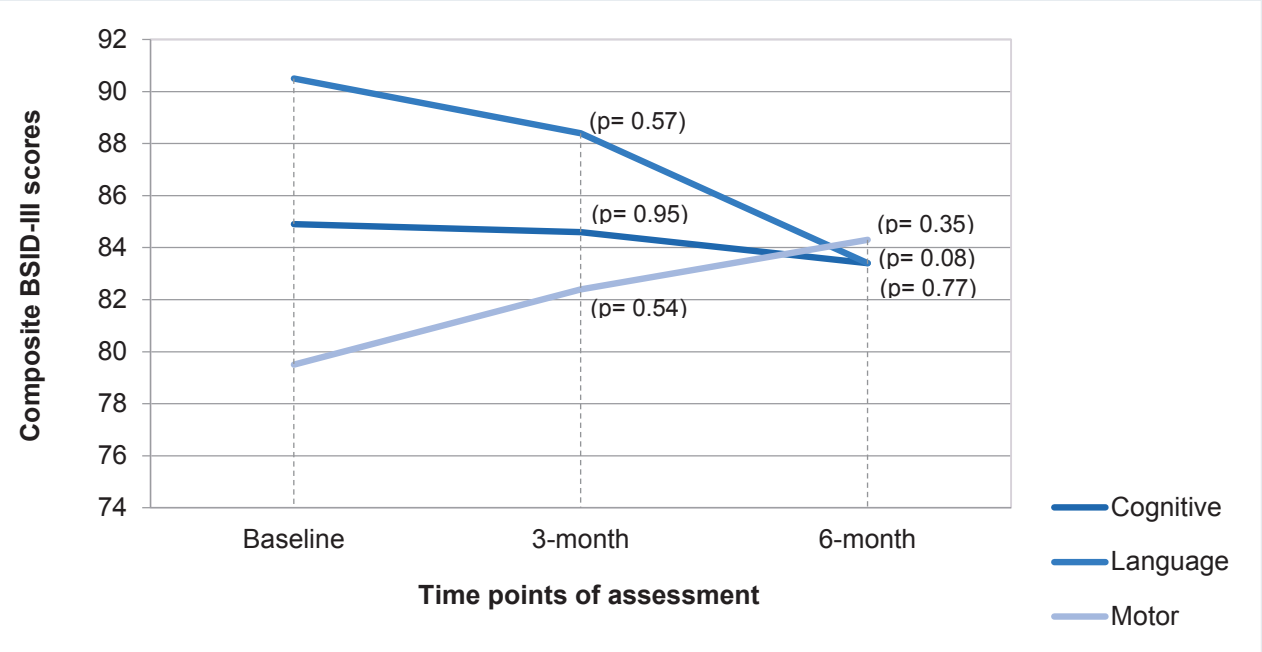

Figure 5.4 Mean composite BSID- III subscale scores across the study

Mean cognitive, language and motor composite scores were below the mean score of 100 across all three of the subscales of the BSID-III at all three of the time points of assessment.

Motor development was the area of weakest developmental performance at baseline. There was improvement in the mean composite scores for motor performance from before to after cardiac intervention. To the contrary, developmental performance of the participants on the language and cognitive subscale declined from baseline to three-month and six-month post-cardiac intervention. The significance of the change in neurodevelopmental performance over time is formally presented and commented on in section 5.11.

Developmental outcomes at each assessment and within each subscale of the BSID-III (cognitive, language, and motor) were furthermore classified as “average” if they were within 1 SD of the mean or higher (scores > 85), “at risk” if they were 1 to 2 SD below the mean (scores of 70–84), and “delayed” if they were >2 SD below the mean (scores <70).

The classification of developmental performance for each of the subscales on the BSID-III is presented in Table 5.15. Values reported are frequencies with percentages.

Table 5.15 Classification of developmental performance

Variable	Baseline (n=40)	Three-month follow-up (n=25)	Six-month follow-up (n=22)
COGNITIVE DEVELOPMENT			
Average or above	23 (57.5%)	17 (68%)	14 (63.6%)
At risk	9 (22.5%)	3 (12%)	2 (9.1%)
Developmentally delayed	8 (20%)	5 (20%)	6 (27.3%)
LANGUAGE DEVELOPMENT			
Average or above	28 (70%)	14 (56%)	9 (40.9%)
At risk	7 (17.5%)	9 (36%)	7 (31.8%)
Developmentally delayed	5 (12.5%)	2 (8%)	6 (27.3%)
MOTOR DEVELOPMENT			
Average or above	19 (47.5%)	15 (60%)	12 (54.5%)
At risk	10 (25%)	4 (16%)	4 (18.2%)
Developmentally delayed	11 (27.5%)	6 (24%)	6 (27.3%)

According to the BSID-III criteria, a developmental delay is categorised at a composite score on any subscale below 2 SD of the mean score of 100 (score of less than 70). At baseline, 14 participants (35%) presented with a developmental delay in at least one area of development. Of the participants with delayed development, five participants (12.5%) had delays in two or more areas of development. Motor delays were the most prevalent, with 11 participants (27.5%) presenting with motor delays before cardiac intervention. The severity of the developmental delays was mild to moderate in most cases; however, four of the

participants' with motor delays (36.4%) had severe delays scoring below 3 SD from the mean (a score of less than 55). Cognitive delays followed by language delays were less prevalent and moderate in severity.

At three-months post-cardiac intervention, six participants (24%) presented with developmental delay in at least one area of development, of these participants with delayed development, four participants (16%) had delays in two or more areas of development. Motor delays remained the most prevalent delay; with six participants (24%) presenting with delayed motor development, and in four of the participants with motor delays (66.7%) the delay was found to be severe. Cognitive followed by language delays were less prevalent and moderate in severity.

At six-month post-cardiac intervention, six participants (27.3%) presented with a developmental delay in at least one area of development. Of the participants with delayed development, five participants (22.7%) had delays in two or more areas of development. The prevalence of developmental delays at this time point was found to be the same across all three of the subscales of the BSID-III. An increase in the prevalence of cognitive and language delays was noted. The prevalence of motor delays remained consistent across study, at above 24%. Six participants presented with motor delays, 50% of who presented with moderate delays and the other 50% with severe delays. All cognitive and language delays were moderate in severity.

A summary of the average prevalence of developmental delays across the study is presented in Figure 5.5.

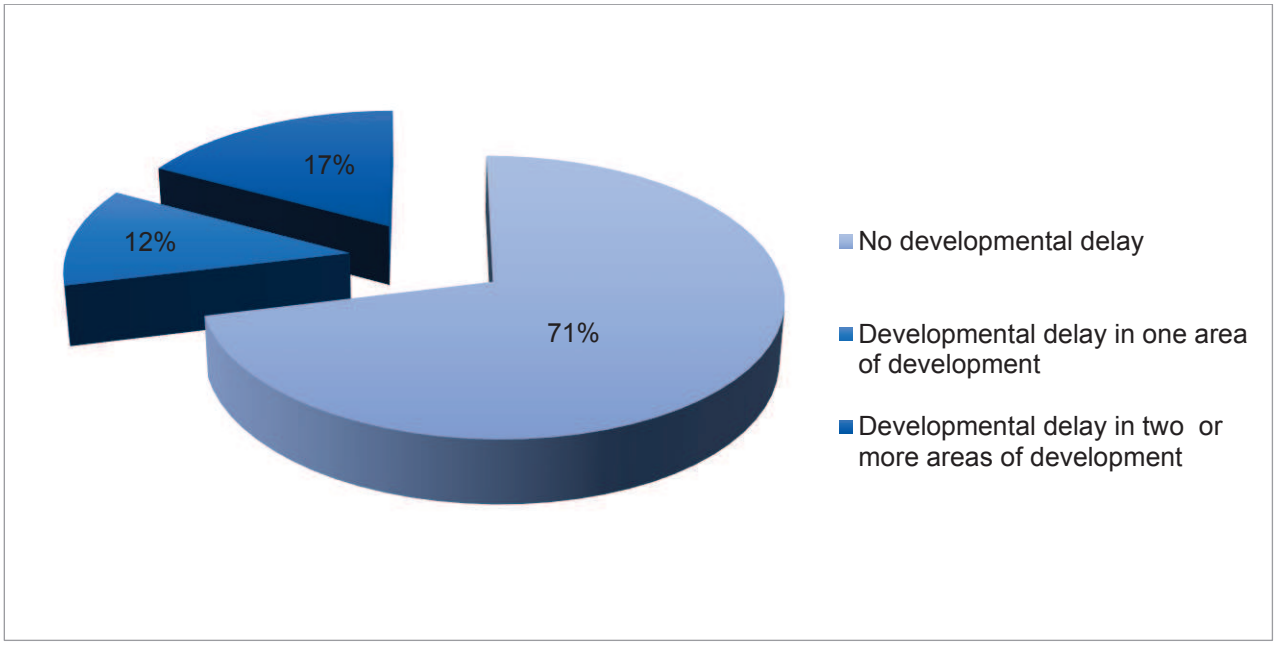

Figure 5.5 Average prevalence of developmental delays across the study

The median age at the time of first cardiac surgery was 7.4 months, making development in the prone position of particular interest in the current study participants, as typically-developing children would start to crawl between the ages of seven and nine months (Bayley, 2006a). Twenty-three participants (57.5%) exhibited delayed prone development, especially with regards to crawling. A median sternotomy was used as the route of surgical access in 78.3% of the children who exhibited delayed prone development. Development in prone was delayed in all participants with DS.

One participant suffered a thrombotic stroke post-cardiac surgery resulting in dense left hemiplegia. The neurological deficit significantly impaired the participant's developmental performance across all three subscales of the BSID-III post-cardiac intervention.

In addition, the BSID-III scores can be used to identify children who would qualify for EI services. This criteria for determining eligibility for EI services is applied in clinical practice in developed countries, as recommended by the AHA in their scientific statement regarding the management of children with CHD (Marino et al., 2012). Children who score below 1 SD of the mean (score of less than 85) on any of the BSID-III subscales (cognitive, language and motor) would qualify for referral to the appropriate EI services. This would therefore include both children at risk of, and those presenting with developmental delays.

This analysis was deemed critical in identifying the need for EI services in this sample, and the type of therapeutic services that would be required. Information about participants qualifying for EI services based on BSID-III performance is presented in Table 5.16. Values reported are frequencies with percentages.

Table 5.16 Children qualifying for early intervention services based on developmental performance

Subscale	Baseline (n=40)	3-months post-cardiac intervention (n=25)	6-months post-cardiac intervention (n=22)
	Frequency (%)	Frequency (%)	Frequency (%)
Cognitive (OT)	17 (42.5%)	8 (32%)	8 (36.4%)
Language (ST)	12 (30%)	11 (44%)	13 (59%)
Motor (PT)	22 (55%)	10 (40%)	10 (45.5%)

* Criteria for EI services is a subscale composite score > 1 SD below the mean score of 100 (Subscale score <85)

The need for access to EI services varied at the various time points of assessment, and is shown in Table 5.16. Figure 5.6 provides a summary of the total need for access to and the type of EI services required.

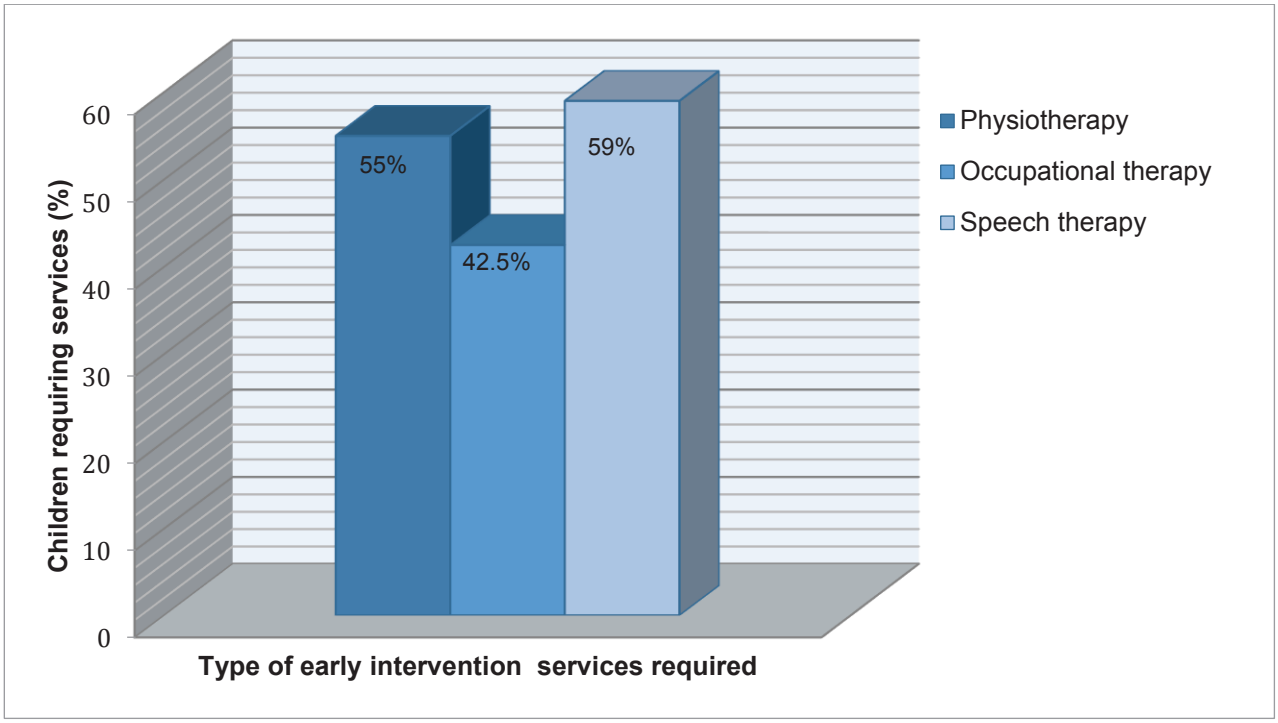

Figure 5.6 Children qualifying for early intervention services

Applying the eligibility criteria for referral to EI serviced based on developmental performance on the BSID-III, it was determined that up to 59% of participants would qualify for EI services over the study period. Of these children, up to 42.5% would require access to OT, 59% to ST, and 55% to PT services over the study period. In many instances, children would require access to multiple therapy services in order to address their risk of developmental delays or delays present in more than one area of development. It is also clear that over time the need for OT and PT services declined slightly; to the contrary, the need for ST services increased over time.

Fifteen participants (37.5%) were referred to, or were accessing EI services to address identified developmental delays. Eight participants (20%) were referred to PT, ten participants (25%) to OT and three participants (7.5%) to ST services.

Parents and children accessing EI services in this study reported that staff constraints within the RSA-DoH often resulted in infrequent therapy appointments and lack of access to specific therapy services, in particular ST. Furthermore, financial and time constraints on the part of parents prevented them from being able to access therapy services. This culminated in the ineffective provision of EI services to the most needy of participants in this

study. The development of a home-based parent-driven developmental stimulation programme to meet the developmental needs of children with CHD in central SA could serve to meet the needs in resource-poor setting. The development of the developmental activity programme, based on the developmental outcomes, is presented in Chapter seven.

5.7 Neurological findings

The only significant finding during the neurological examination at baseline, and at three-month and six-month post-cardiac intervention was the presence of abnormal muscle tone. Findings regarding abnormal muscle tone are presented in Table 5.17. The values reported are frequencies with percentages.

Table 5.17 Presence of abnormal muscle tone

Distribution of muscle tone	Baseline (n=40)	Three-months post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Hypotonia	18 (45%)	11 (44%)	7 (31.8%)
Normal muscle tone	21 (52.5%)	14 (56%)	15 (68.2%)
Hypertonia	1 (2.5%)	0	0

Forty-five percent and 44% of the participants presented with hypotonia at baseline and at three-month post-cardiac intervention respectively. All participants with DS presented with marked hypotonia at all three time points of assessment. Twenty percent of participants without genetic comorbidity presented with hypotonia at baseline, 24% at the three-month post-cardiac intervention and 9.1% at the six-month post-cardiac intervention. Hypotonia seemed to increase in the period initially following cardiac surgery, but in most cases tended to resolve over time in participants without DS.

The single case of hypertonia noted at baseline appeared to be transient and resolved spontaneously post-cardiac intervention.

5.8 Parents' perception of health-related quality of life

HRQOL was determined using the PedsQL™ Infant Scales for children under the age of two years and the PedsQL™ Cardiac Module for participants older than two years. At baseline all participants were younger than two years and their HRQOL outcomes are reported for the PedsQL™ Infant Scales.

At three-month post-cardiac intervention, one participant, and at six-months post-cardiac intervention four participants respectively were older than two years and their HRQOL outcomes were reported for the PedsQL™ Cardiac Module.

HRQOL outcomes at baseline, and at three-month and six-month post-cardiac intervention for children younger than two years on the PedsQL™ Infant Scales are reported in Table 5.18. Values reported are medians with ranges and means with standard deviations. The subscales of the PedsQL™ Infant Scales were used to calculate the summary scale score and the total score. Values are reflected as a score out of 100. Higher scores are indicative of better-perceived HRQOL.

Table 5.18 Perceived health-related quality of life of children one to 24 months

Subscales	Baseline (n=40)	Three-months post-cardiac intervention (n=24)	Six-months post-cardiac intervention (n=18)
Physical functioning			
Median (range)	83.3 [16.7 – 100]	100 [37.5 – 100]	100 [33 – 100]
Mean and SD	76.5 (± 21.4)	91.4 (±17.4)	88.5 (±18.7)
Physical symptoms			
Median (range)	80 [35 – 100]	90 [45 – 100]	88.8 [50 – 100]
Mean and SD	76.4 (± 15.9)	86.4 (± 13.6)	84.6 (±13.2)
Emotional symptoms			
Median (range)	75 [16.7 – 100]	82.3 [25 – 100]	81.5 [62.5 – 100]
Mean and SD	70.8 (±17.8)	77.3 (±20.3)	87.5 (± 10.9)
Social functioning			
Median (range)	100 [50 – 100]	100 [0 – 100]	100 [62.5 – 100]
Mean and SD	94.8 (± 12.4)	90.9 (±23.04)	94.3 (±11.5)
Cognitive functioning			
Median (range)	100 [37.5 – 100]	100 [0 -100]	100 [25 – 100]
Mean and SD	88.1 (±19.1)	87.3 (±26.8)	83.7 (± 23.4)
SUMMARY SCALES FOR THE PEDSQL® INFANT MODULES AS CALCULATED FROM THE ABOVE SUBSCLAES			
Psychological health			
Median (range)	78.2 [48.8 – 100]	90.6 [20 – 100]	84.7 [59.6 – 100]
Mean and SD	78.3 (±12.4)	82.6 (±19.9)	83.4 (± 11.7)
Physical health			
Median (range)	79.7 [29.7 – 97.4]	91.5 [42.2 – 100]	89.1 [42.1 – 100]
Mean and SD	76.8 (± 16.6)	88.3 (± 14.2)	86.0 (± 14.2)
Total HRQOL score			
Median (range)	80.6 [48.8 – 97.2]	89.6 [29.9 – 100]	87.9 [52.2 – 100]
Mean and SD	77.6 (± 12.4)	85.2 (± 16.1)	85.1 (±11.2)

Parents of children younger than two years perceived their child's HRQOL as good at all three of the assessment time points. Parents' perception of their children's HRQOL improved post-cardiac intervention, as reflected by both the mean and median total scores. At baseline, parents perceived their children's physical health as being poorer than their psychosocial health, whereas post-cardiac intervention the converse tended to be true.

HRQOL outcomes at baseline, and three-month and six-month post-cardiac intervention for children older than two years as reported on the PedsQL™ Cardiac Module are presented in Table 5.19. Values reported are medians with ranges and means with standard deviations.

The PedsQL™ Cardiac Module does not formally report calculating a total score, total scores have been calculated in previous studies using the PedsQL™ cardiac module for example Sand et al. (2013). The same principle as applied by Sand et al. (2013) has been applied in this study to generate a total score. A total score was calculated for determining HRQOL across all participants in this study sample across the three modules of the PedsQL™ that were used. The Subscales were used to calculate the total score on the PedsQL™ Cardiac Module. Values are reflected as a score out of 100. Higher scores are indicative of better-perceived HRQOL.

Table 5.19 Perceived health-related quality of life of children older than two years

Subscales	Three-months post-cardiac intervention (n=1)	Six –months post-cardiac intervention (n=4)
Heart symptoms		
Median (range)		100 [95 – 100]
Mean and SD	95	98.8 (±2.5)
Perceived physical appearance		
Median (range)		100 [83.3 – 100]
Mean and SD	100	95.8 (± 8.4)
Treatment anxiety		
Median (range)		62.5 [0 – 100]
Mean and SD	100	56.3 (±50.5)
Cognitive problems		
Median (range)		100 [16.3 – 100]
Mean and SD	100	79.1 (±41.8)
Communication		
Median (range)		100 [0 – 100]
Mean and SD	100	75.0 (±50.0)
Total score		
Median (range)		82.6 [76.1 – 100]
Mean and SD	97.8	85.3 (± 10.4)

Parents of children aged two years and older perceived their children's post-cardiac intervention HRQOL as good at both time points the measure was utilised. For some older children, treatment anxiety became a concern as they became older. Similar to the findings on the PedsQL™ Infant Modules post-cardiac intervention levels of cognitive and language functioning became of greater concern to parents than physical functioning over time.

The PedsQL™ Infant Module and the PedsQL™ Cardiac Module outcomes are comparable as measures of perceived HRQOL in children with CHD. Total scores across the PedsQL™

Infant Modules and the PedsQL™ Cardiac Module were combined and analysed to reflect the perceived HRQOL for all participants. Values reported are reflected as a score out of 100. Higher scores are indicative of better-perceived HRQOL. The perceived HRQOL for all participants is presented in Table 5.20. Values reported are medians with ranges and means with standard deviations.

Table 5.20 Perceived health-related quality of life for all children

Variable	Baseline (n=40)	Three-months post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Total score			
Median (range)	80.6 [48.6 – 97.2]	90.3 [29.9 – 100]	86.7 [52.2 – 100]
Mean and SD	77.6 (±12.4)	85.7(±15.9)	85.1 (±10.8)

Figure 5.7 shows a graphical representation of the mean total HRQOL scores at all three time-points of assessment for descriptive purposes.

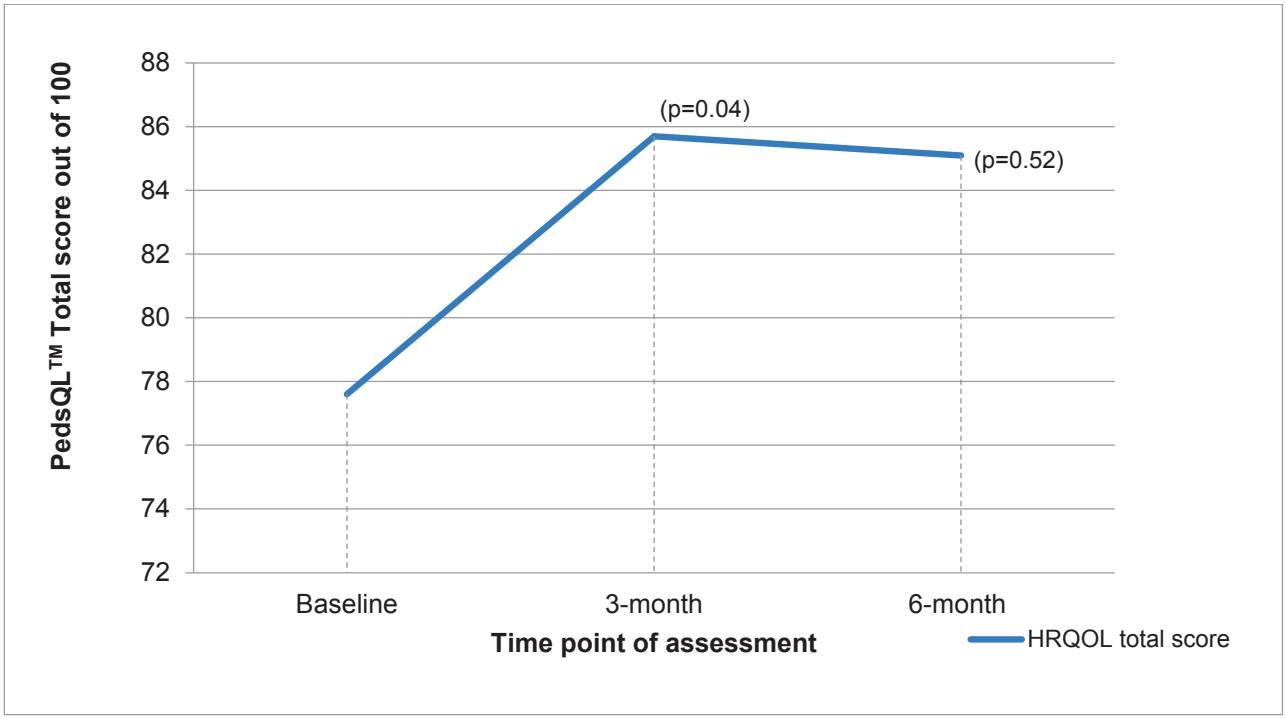

Figure 5.7 Mean PedsQL™ total scores across the study

Parents of all participants perceived their children's HRQOL as good at all three time points of assessment, both before and after cardiac intervention. Parent's perception of their children's HRQOL improved after cardiac intervention as indicated by both mean and median total HRQOL scores. Perceived HRQOL remained similar at three-month and six-month post-cardiac intervention. The significance of the change in HRQOL over time is formally presented and commented on in section 5.11.

Parents however had wide ranging perceptions of their children's HRQOL at all three assessment time points, both before and after cardiac intervention. Some parents viewed their children's HRQOL as exceptionally poor whilst others viewed it as excellent.

5.9 Parenting stress outcomes

Parenting stress of the primary caregivers was established for all participants using the PSI-SF. Parenting stress was reported by mothers with the exception of a single case where the father fulfilled the role of primary caregiver.

Parenting stress is reported across three subscales, namely parenting distress, parent-child-dysfunction and difficult child. A total stress score was also calculated. Parenting stress scores for the subscales and total stress scores are reflected as percentiles. Values provided are medians with ranges and means with SD. Levels of distress experienced by primary caregivers are reflected in Table 5.21.

Table 5.21 Parenting stress of the primary caregivers

PSI-SF Scales	Baseline (n=40)	Three-month post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Parenting distress			
Median (range)	90 [10-99]	75 [1 – 95]	65 [1 – 95]
Mean and SD	83.3 (±19.9)	63.8 (±31.9)	57.8 (±31.9)
Parent-child dysfunction			
Median (range)	90 [40 – 99]	85 [5 – 99]	80 [5 – 99]
Mean and SD	80 (±19.8)	72.8 (±27.2)	63.5 (±34.2)
Difficult child			
Median (range)	77.5 [1 – 99]	55 [1 – 95]	47.5 [1 – 95]
Mean and SD	67.1 (±26.3)	52.6 (±27.6)	47.6 (±35.5)
Total stress			
Median (range)	90 [5 – 99]	80 [1 – 99]	67.5 [1 – 99]
Mean and SD	83.8 (±19.2)	69 (±28.5)	57.8 (±34.8)

Percentile scores over all three subscales and for the total stress can be used to classify the extent to which parents are experiencing stress. Scores across all subscales above the 85th percentile are considered to be high. For the parent-child dysfunctional interaction, a subscale score above the 85th percentile is considered clinically significant and for the other subscales of parental distress, difficult child and the total stress scores above the 90th

percentile are considered clinically significant. Normal scores lie between the 15th and 80th percentile, and scores are considered low if below the 15th percentile.

The classification of the levels of parenting stress experienced by parents in this study sample is presented in Table 5.22 (see table on the following page).

Table 5.22 Classification of the levels of parenting stress

Subscales of the PSI-SF	Baseline (n=40)	Three-months post-cardiac intervention (n=25)	Six-months post-cardiac intervention (n=22)
Parenting distress			
Clinically significant	24 (60%)	7 (28%)	5 (22.7%)
High	31 (77.5%)	11 (44%)	7 (31%)
Normal	8 (20%)	11 (44%)	12 (54.4%)
Low	1 (2.5%)	3 (12%)	3 (13.7%)
Parent-child dysfunction			
Clinically significant	22 (55%)	11 (44%)	9 (40.9%)
High	22 (55%)	13 (52%)	9 (40.9%)
Normal	18 (45%)	11 (44%)	10 (45.5%)
Low	0 (0%)	1 (4%)	3 (13.6%)
Difficult child			
Clinically significant	7 (17.5%)	3 (12%)	3 (13.6%)
High	14 (35%)	4 (16%)	5 (22.7%)
Normal	24 (60%)	19 (76%)	11 (50%)
Low	2 (5%)	2 (8%)	6 (27.3%)
Total stress			
Clinically significant	24 (60%)	6 (24%)	7 (31.8%)
High	27 (67.5%)	9 (36%)	7 (31.8%)
Normal	12 (30%)	14 (56%)	11 (50%)
Low	1 (2.5%)	2 (8%)	4 (18.2%)

> 85th percentile (high), >90th percentile clinically significant, 15th – 80th percentile (normal), <15th percentile (low)

The mean total stress scores at all time points of assessment are presented graphically in Figure 5.8 for descriptive purposes.

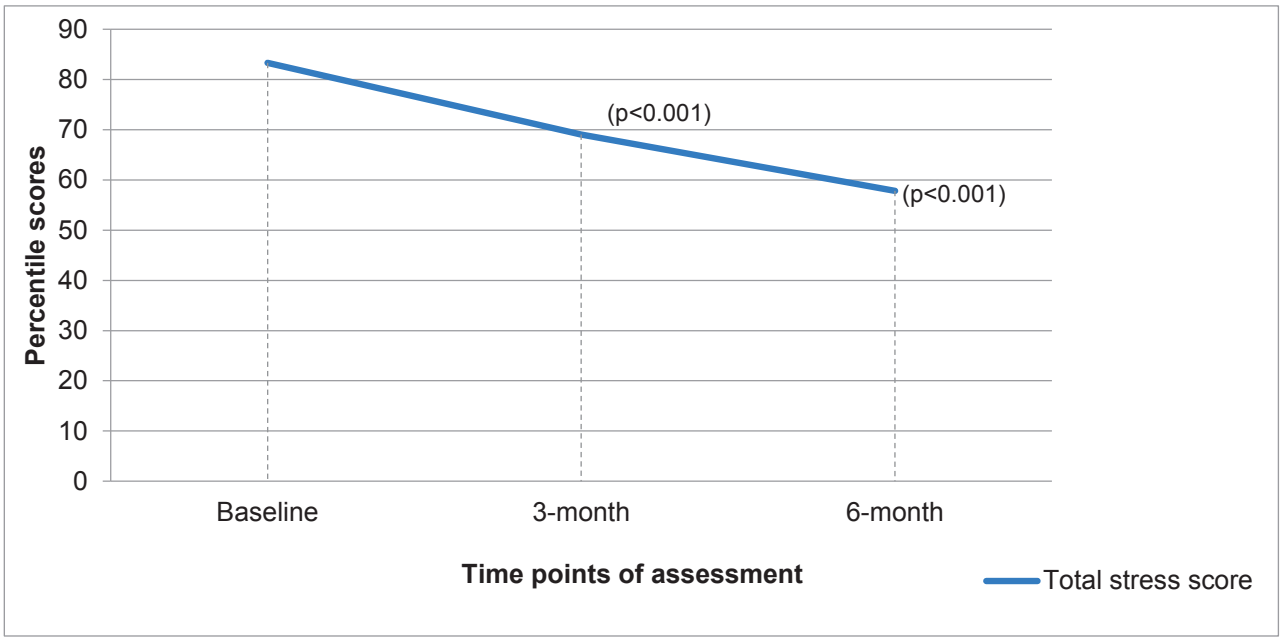

Figure 5.8 Mean total stress scores across the study

The majority of primary caregivers (60%) experienced clinically significant levels of stress in their parenting role at baseline as reflected by the scores on the PSI-SF scales and the total stress score. More than half of the primary caregivers felt that their child failed to meet their expectations (reflected by scores on the parent-child dysfunction subscale). Most parents however felt that their children were not difficult to parent (reflected by scores on the difficult child subscale). Several parents of children older than two years noted concerns about their child's behaviour. These concerns included tantrums, inattention and hyperactivity. However, behaviour was not formally assessed as part of the neurodevelopmental assessment due to the age profile of this study's participants.

The levels of parenting distress and role stress declined post-cardiac intervention, and continued to decline over time; most parents then experienced normal levels of stress. Dysfunction in parent-child interaction also improved over time, but it remained the aspect that continued to contribute most to the levels of parenting stress over time. The significance of the change in the levels of parenting stress over time is formally presented and commented on in section 5.11.

The PSI-SF only reflects levels of parenting stress directly related to the primary caregiver's parenting role. Anecdotal reports provided by many of the primary caregivers in this study indicate that unemployment, low SES, low levels of education and a lack of social support may further exacerbate the stress they are already experiencing in their parenting role.

5.10 Burden of care

Parents reporting on the number of times their child was hospitalised determined the burden of care placed on the primary caregiver, and the effect their child's health had on their work life and daily routine. This descriptive information served as a reflection of the magnitude of the care burden experienced by primary caregivers in this study sample. The burden of care experienced by the primary caregivers across the study is summarised in Table 5.23. Values reported are medians with ranges and means with standard deviations.

Table 5.23 Burden of care across the study

Variables	Before cardiac intervention (n=40)	Between hospital discharge and three-month follow-up (n=25)	Between three-month and six-month follow-up (n=22)
Number of hospital admissions			
Median (range) Mean and SD	2 [0 – 5] 2. 02 (±1.31)	0 [0 – 2] 0.2 (±0.5)	0 [0 - 1] 0.2 (±0.4)
Number of days child too ill to play			
Median (range) Mean and SD	0 [0 – 21] 1.5 (±3.7)	0 [0 – 5] 0.4 (±1.2)	0 [0 – 14] 1.2 (±3.3)
Number of days child required special care			
Median (range) Mean and SD	0 [0 -31] 5 (±9.6)	0 [0 -3] 0.3 (±0.9)	0 [0 – 14] 1.2 (± 3.3)

* Hospitalisations excluded the admission for cardiac intervention

The majority of the participating children (87.5%) had at least one hospital admission prior to cardiac intervention. Participants tended to have far fewer hospital admissions post-cardiac intervention. The main reason for hospital admissions both before and after cardiac intervention was respiratory-related complications.

Twenty percent of the primary caregivers were employed at the time of their child's first cardiac intervention. In some instances, primary caregivers reported having to miss work due to their child's ill health. For the majority of employed primary caregivers, their child's health did not affect their work routine and ability to concentrate at work as a carer looked after the child during the workday. In the case of working mothers, the grandmothers carried a heavy burden of care.

Ten percent of the primary caregivers were either learners or students at the time of their children's first cardiac surgery. They reported that their children's ill health affected their school and class attendance prior to cardiac intervention, but this was no longer the case post-cardiac intervention. Grandmothers carried a heavy caregiving burden in cases where the mother was a learner, student or teenager, or where the father was the primary caregiver.

The majority of primary caregivers were housewives at the time of their child's first cardiac intervention, either out of choice to care for their child, or due to the inability to find gainful employment. They reported that their child's health affected their ability to continue with daily chores within the home prior to cardiac intervention, but this was seldom the case post-cardiac intervention.

Two mothers and one father gave up their employment post-cardiac intervention to play a more active role in the caregiving of their children. However, this came at a financial cost to the families. Many mothers reported a desire to seek gainful employment after their child's cardiac intervention as a result of their children's improved health and the diminished care burden.

It is therefore evident that caring for a child with CHD heightened the financial, emotional and physical burden of care for both parents and grandparents, in many instances. The

burden of care predominantly fell on mothers in this study sample. The burden of care was greater prior to cardiac intervention, and declined post-cardiac intervention and over time as the children's health status improved.

5.11 Changes in key outcomes over time

Within the group, changes in key outcomes over time, including growth, neurodevelopment, HRQOL and parenting stress over time were calculated using a 95% confidence intervals for the difference between the z-score means. Testing was done at the 0.05 level of significance. Data from all participants assessed at the various time-points was included in the analysis.

The changes in key outcomes over time are presented in Table 5.24.

Table 5.24 Changes in key outcomes over time

Outcome	Z-score means			Three-months vs. Baseline		Six-months versus Baseline	
	Mean: Baseline (n=40)	**Mean: Three- month (n=25)**	**Mean: Six- month (n=22)**	**95% CI**	**p-value**	**95% CI:**	**p-value**
Growth parameters							
WAZ	-2.540	-1.844	-1.634	-0.098; 1.490	0.09	0.063; 1.749	0.04*
HAZ	-2.185	-1.553	-1.795	-0.516; 1.780	0.28	-0.779; 1.558	0.51
HCAZ	-1.345	-0.864	-0.350	-0.337; 1.299	0.25	0.138; 1.852	0.02*
BSID-III composite scores							
Cognitive	6.975	6.920	6.682	-1.923; 1.813	0.95	-2.289 ; 1.703	0.77
Language	16.700	15.960	14.364	-3.331; 1.851	0.57	-4.991 ; 0.318	0.08
Motor	13.150	14.120	14.773	-2.145; 4.085	0.54	-1.801 ; 5.047	0.35
HRQOL							
PedsQL™ total scores	77.643	85.163	80.589	0.345; 14.695	0.04*	-6.108; 12.002	0.52
Parenting stress							
PSI-SF total score	37.200	18.850	15.650	-24.115; -12.585	<0.001***	-27.131;-15.969	<0.001***
Neurological status							
Muscle tone	1.500	1.440	1.318	-0.334; 0.214	0.66	-0.463; 0.099	0.20

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001 (WAZ = weight-for-age z-score; HAZ= height-for-age z-score; HCAZ= head circumference-for-age z-score

Statistically significant changes were seen in three of the four key outcomes, including growth, HRQOL and parenting stress from before cardiac intervention to post-cardiac intervention.

Significant catch-up growth was seen for both weight and head circumference at six-month post-cardiac intervention when compared to growth prior to cardiac intervention. The significant improvement in head circumference suggests that the small head size was related to the growth failure rather than small brain volume. There was also a significant improvement in parents' perception of their children's HRQOL at three-month post-cardiac intervention when compared with their perceived HRQOL prior to cardiac intervention.

Levels of parenting stress were found to have declined significantly from before cardiac surgery at both three-month and six-months post-cardiac intervention when compared to levels of parenting stress prior to cardiac intervention.

Change in neurodevelopmental outcomes and muscle tone over time were not found to be significant.

5.12 Variables associated with key outcomes

Variables known to be risk factors for adverse developmental outcome and poorer HRQOL, as well as those associated with increased levels of parental distress were analysed for various sub-categories for their association with key outcomes by means of ANOVAs. The results of the variables analysed as main effects for each of the key outcomes, namely neurodevelopment, HRQOL and parenting stress, are presented below. The main effects in the model represent the multiple factors influencing the response in each of the named categories.

A regression analysis was also done using ANOVAs to determine variables predictive of key outcomes. Only the findings for associations will be presented in the results section.
The results of the regression analysis can be referenced in Appendix XIV.

5.12.1 Variables associated with neurodevelopmental outcome

Variables that demonstrated an association with neurodevelopmental outcome were determined for individual variable sub-categories at baseline, and at three-month and six-month post-cardiac intervention.

Variables associated with each of subscales of the BSID-III (cognitive, language and motor) are presented in Table 5.25 to 5.27 (See tables on the pages to follow). These variables were set as main effects in the ANOVA models.

Table 5.25 Variables associated with the BSID-III cognitive scores

Variables for BSID-III cognitive scores	P-values			Change in z-score means for BSID-III cognitive scores for significant associations			
	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Trend direction
Type and severity of CHD				84.1	6.9	6.7	Decreasing cognitive scores
Disease severity	0.02*	0.96	0.96				
Type CHD	0.24	0.41	0.08				
Surgery and medical course							
Age at time of first surgery	0.15	0.24	0.70				
CPB time	0.53	0.89	0.37				
Post-operative complications	0.91	0.49	0.20				
Duration of mechanical ventilation	0.62	0.13	0.15				
Hospital and ICU length of stay							
ICU length of stay	0.23	0.23	0.24				
Hospital length of stay post-surgery	0.70	0.67	0.71				
Patient factors							
Gender	0.99	0.68	0.57				
Prematurity	0.23	0.62	0.63				
Low birth weight	0.17	0.89	0.95				
Genetic comorbidity (DS)	0.00***	0.00***	0.00****				
Growth (weight-for-age)	0.32	0.49	0.26				
Sociodemographic factors							
Distance to cardiac service point	0.25	0.40	0.54				
Age of mother	0.01*	0.01**	0.01**				
Level of education of mother	0.69	0.05	0.30				
Socioeconomic status	0.89	0.95	0.75				

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Disease severity only showed a significant association with cognitive outcome prior to cardiac intervention. The presence of a genetic comorbidity (DS) and maternal age were significantly associated with cognitive developmental outcome prior to cardiac intervention, as well as at three-month and six-month post-cardiac intervention. All significant values are due to a decrease in cognitive scores.

Table 5.26 Variables associated with the BSID-III language scores

Variables for BSID-III language scores	P-values			Change in z-score means for BSID-III language scores for significant associations			
	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Trend direction
Type and severity of CHD				90.5	16.0	14.4	Decreasing language scores
Disease severity	0.62	0.06	0.94				
Type CHD	0.47	0.85	0.63				
Surgery and medical course							
Age at time of first surgery	0.00**	0.04*	0.11				
CPB time	0.87	0.36	0.70				
Post-operative complications	0.29	0.55	0.81				
Duration of mechanical ventilation	0.51	0.25	0.87				
Hospital and ICU length of stay							
ICU length of stay	0.60	0.87	0.85				
Hospital length of stay post-surgery	0.21	0.22	0.44				
Patient factors							
Gender	0.59	0.69	0.88				
Prematurity	0.09	0.54	0.69				
Low birth weight	0.95	0.92	0.51				
Genetic comorbidity (DS)	0.00**	0.00**	0.00**				
Growth (weight-for-age)	0.06	0.11	0.48				
Sociodemographic factors							
Distance to cardiac service point	0.23	0.19	0.37				
Age of mother	0.25	0.26	0.17				
Level of education of mother	0.45	0.89	0.26				
Socioeconomic status	0.68	0.76	0.95				

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

The presence of a genetic comorbidity (DS) was shown to be the variable significantly associated with language development outcomes both prior to and after cardiac intervention. Age at the time of first cardiac intervention was also significantly associated with language development outcomes prior to cardiac intervention and at three-month post-cardiac intervention. All significant values are due to a decrease in language scores.

Table 5.27 Variables associated with the BSID-III motor scores

Variables for BSID-III motor scores	P-values			Change in z-score means for BSID-III motor scores for significant associations			
	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Trend direction
Type and severity of CHD				79.5	16.0	14.8	Decreasing motor score
Disease severity	0.63	0.93	0.70				
Type CHD	0.86	0.69	0.15				
Surgery and medical course							
Age at time of first surgery	0.62	0.94	0.91				
CPB time	0.49	0.51	0.77				
Post-operative complications	0.23	0.18	0.36				
Duration of mechanical ventilation	0.61	0.07	0.16				
Hospital and ICU length of stay							
ICU length of stay	0.06	0.37	0.21				
Hospital length of stay post-surgery	0.51	0.93	0.84				
Patient factors							
Gender	0.77	0.78	0.90				
Prematurity	0.13	0.96	0.70				
Low birth weight	0.82	0.32	0.31				
Genetic comorbidity (DS)	0.00***	0.00***	0.00***				
Growth (weight-for-age)	0. 04*	0.20	0.40				
Sociodemographic factors							
Distance to cardiac service point	0.97	0.33	0.97				
Age of mother	0.03*	0.01**	0.00***				
Level of education of mother	0.91	0.32	0.41				
Socioeconomic status	0.29	0.29	0.32				

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Growth prior to cardiac intervention was significantly associated with motor performance at baseline. The presence of DS and maternal age were significantly associated with motor development outcomes both before and after cardiac surgery. All significant values are due to a decrease in motor scores.

5.12.2 Variables associated with parents' perception of health-related quality of life

Variables that demonstrated an association with parent perceived HRQOL were determined for individual variable sub-categories at baseline, and at three-month and six-month post-cardiac intervention.

Variables associated with PedsQL^{TM} total scores are presented in Table 5.28. These variables were set as main effects in the ANOVA models.

Table 5.28 Variables associated with parents' perception of health-related quality of life

Variables for PedsQL™ total scores	P-values			Change in z-score means for PedsQL™ total scores for significant associations			
	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Trend direction
Disease type and severity				77.6	81.0	80.6	Increase in PedsQL™ total scores
Disease severity	0.09	0.80	0.97				
Type CHD	0.76	0.42	0.57				
Peri-operative risk factors							
Age at surgery	0.25	0.11	0.06				
CPB time	0.10	0.59	0.97				
Patient factors							
Genetic comorbidity (DS)	0.53	0.49	0.83				
Growth (weight-for-age)	0.96	0.51	0.82				
Feeding problems	0.13	0.59	0.58				
Sociodemographic factors							
Age of mother	0.17	0.97	0.72				
Level of maternal education	0.42	0.37	0.25				
Socioeconomic status	0.64	0.46	0.53				
Neurodevelopmental outcome							
Cognitive development	0.36	0.79	0.86				
Language development	0.13	0.64	0.38				
Motor Development	0.01*	0.84	0.93				
Parenting stress							
PSI-SF total stress score	0.02*	0.08	0.97				

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Motor developmental performance and levels of parenting stress prior to cardiac intervention were shown to have a significant association with parental perception of their child's HRQOL. None of the categories of variables were shown to be predictive of HRQOL after cardiac intervention. All significant values are due to an increase in PedsQL^{TM} total scores.

5.12.3 Variables associated with levels of parenting stress

Variables that demonstrated an association with levels of parenting stress were determined for individual variable sub-categories at baseline, and at three-month and six-month post-cardiac intervention.

Variables associated with PSI-SF total scores are presented in Table 5.29. These variables were set as main effects in the ANOVA models.

Table 5.29 Variables associated with levels of parenting stress

Variables for PSI-SF total score	P-values			Change in z-score means for PSI-SF total scores for significant associations			
	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Baseline	Three-months post-cardiac intervention	Six-months post-cardiac intervention	Trend direction
Disease type and severity				37.2	30.2	28.5	Decreasing PSI-SF total score
Disease severity	0.39	0.67	0.56				
Type CHD	0.57	0.68	0.61				
Peri-operative risk factors							
Age at surgery	0.11	0.03*	0.43				
Patient factors							
Genetic comorbidity (DS)	0.11	0.41	0.67				
Growth (weight-for-age)	0.89	0.28	0.62				
Feeding problems	0.79	0.69	0.33				
Sociodemographic factors							
Age of mother	0.55	0.04*	0.10				
Level of maternal education	0.07	0.39	0.30				
Socioeconomic status	0.50	0.11	0.12				
Neurodevelopmental outcome							
Cognitive development	0.29	0.94	0.44				
Language development	0.04*	0.03*	0.77				
Motor Development	0.50	0.21	0.19				
Perceived HRQOL							
PedsQL® total score	0.02*	0.08	0.97				

Indication of statistical significance: * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$

Neurodevelopmental outcome, in particular language developmental performance, was significantly associated with levels of parenting stress prior to cardiac intervention and at three-month post-cardiac intervention. Parents' perception of their child's HRQOL prior to cardiac intervention was also found to be significantly associated with levels of parenting stress. In addition, the age of the child at the time of the first cardiac intervention, and the age of the mother, was also associated with levels of parenting stress at three-month post-cardiac intervention. All significant values are due to a decrease in PSI-SF total scores.

It became evident from the analysis that parents' perception of their child's HRQOL was closely related with the level of parenting stress experienced prior to the child undergoing cardiac surgery.

5.13 Key outcomes for groups of special interest

This study aimed to report on outcomes for all participants; however, the outcomes of participants with genetic comorbidity (DS in this study) and those with cyanotic heart defects were still considered to be of special interest.

The limited sample size resulted in small subgroups, which were not sufficiently powered to be able to draw meaningful conclusions from formal statistical analyses of between group differences. Despite this limitation, it was still deemed important to investigate tendencies and trends in outcomes between participants with CHD with DS compared to those with CHD without DS, as well as those with cyanotic heart defects compared to those with acyanotic heart defects for descriptive purposes.

A summary of the most important findings of between group differences for subgroups of special interest will be highlighted in this section. Additional tables of outcomes between subgroups of special interest, namely CHD with DS compared to CHD without DS, and for the cyanotic heart defects compared to acyanotic heart defects can be referenced in Appendix XV and Appendix XVI respectively.

5.13.1 Outcomes for children with CHD with Down syndrome compared to those with CHD without Down syndrome

A quarter of the participants in this study were diagnosed with a genetic comorbidity in addition to their diagnosis of CHD. In all cases, the diagnosed genetic abnormality was DS. The proportion of participants with genetic comorbidity in this study sample is shown in Figure 5.9.

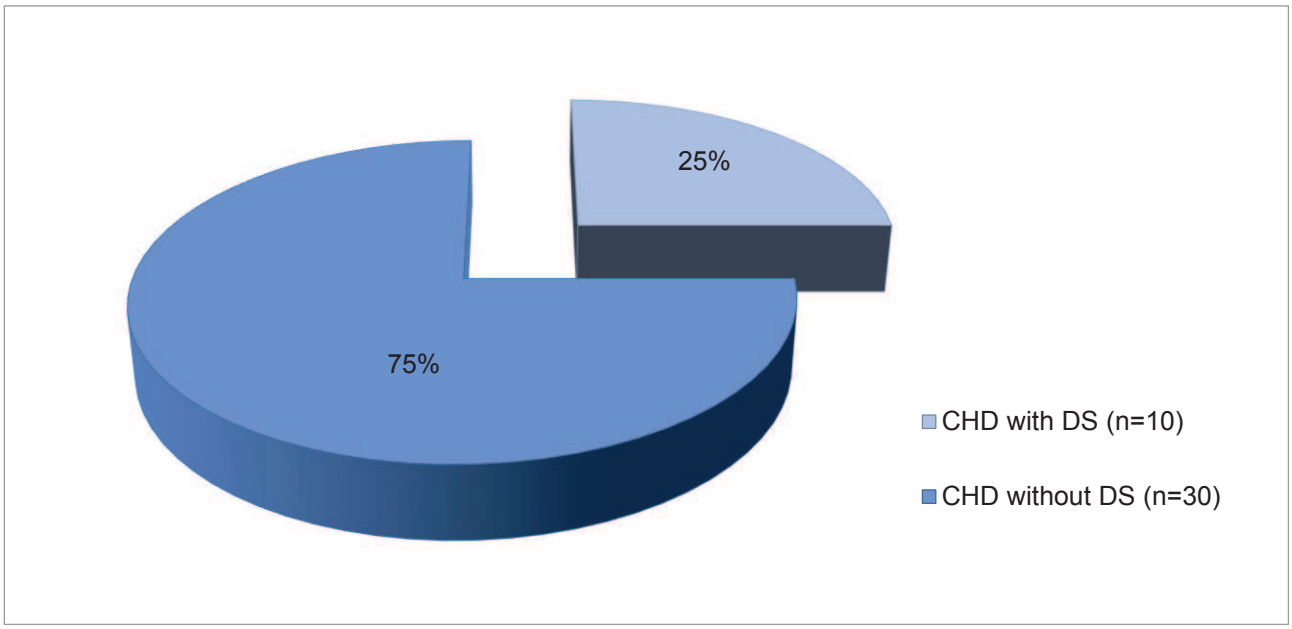

Figure 5.9 Prevalence of Down syndrome in this study sample (n=40)

5.13.1.1 Sociodemographic information

Sociodemographic variables for participants in the subgroup with CHD and DS were similar to that in the group with CHD without DS, apart from maternal age that was more advanced in the group of CHD with DS. The median age was 37 years compared to only 27.5 years in the group with CHD without DS.

5.13.1.2 Cardiology diagnostic information

The type and severity of cardiac disease was similar in both groups. The profile of CHD however varied between groups. AVSDs were the most common primary cardiac diagnosis

in the group of CHD with DS (60%), whilst VSDs were most common in the CHD without DS group (43.3%).

5.13.1.3 Surgical intervention and post-operative medical course

Children in the group of CHD with DS tended to be slightly older at the time of their first cardiac intervention. Surgical variables with regards to duration of CPB, aorta cross-clamp time, length of cardiothoracic ICU stay and post-surgery hospital length of stay were similar in both groups. Post-operative mortality was higher in the group of CHD with DS. Sixty-seven percent of participants who died post operatively had CHD with DS.

5.13.1.4 Growth outcomes

Anthropometric data using the z-score system for weight-for-age, height-for-age and head circumference-for-age at baseline and for the three-month and six month post-cardiac intervention is presented in Table 5.30. Values reported are medians with ranges and means with standard deviations.

Table 5.30 Growth outcomes in children with CHD with DS compared to those with CHD without DS

Growth parameter	CHD and DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Weight-for-age z-score		
Median	-2.6	-2.6
Mean and SD	-2.3 (±1.6)	-2.6 (±1.5)
Height-or-age z-score		
Median	-0.9	-2.0
Mean and SD	-1.5 (±3.0)	-2.4 (±2.3)
Head circumference-for-age z-score		
Median	-1.7	-1.4
Mean and SD	-1.6 (±0.9)	-1.3 (±1.7)
Three-months post-cardiac intervention	**(n=5)**	**(n=20)**
Weight-for-age z-score		
Median	-1.1	-2.2
Mean and SD	-1.1 (±2.6)	-2.0 (±1.4)
Height-for-age z-score		
Median	-1.1	-0.7
Mean and SD	-2.2 (±2.5)	-1.1 (±1.5)
Head circumference-for-age z-score		
Median	-0.9	-1.0
Mean and SD	-1.8 (±1.9)	-0.6 (±1.7)
Six-months post-cardiac intervention	**(n=5)**	**(n=17)**
Weight-for-age z-score		
Median	-1.2	-1.7
Mean and SD	-0.9 (± 2.1)	-1.8 (±1.8)
Height-for-age z-score		
Median	-1.6	-1.5
Mean and SD	-2.1 (±1.4)	-1.7 (±1.7)
Head circumference for age z-score		
Median	-1.6	-1.5
Mean and SD	-2.1 (±1.4)	-1.7 (±1.7)

Growth outcomes for participants in the group of CHD with DS and those in the group of CHD without DS were similar when the growth of participants with DS was determined using the DS-specific growth charts, which allowed for fair comparison with their peers.

The majority of participants in both groups (more than 60%) presented with malnutrition prior to cardiac intervention, a large number of participants in both groups (more than 40%) were also stunted. The prevalence of microcephaly was also high in both groups (more than 20%). Growth across all growth parameters improved in both groups post-cardiac intervention.

5.13.1.5 Neurodevelopmental outcomes

Composite scores for cognitive, language and motor subscales of the BSID-III for both groups are reported in Table 5.31. Values reported are medians with ranges and means with standard deviations.

Table 5.31 Developmental outcomes on the BSID-III for children with CHD with DS compared to those with CHD without DS

Variable	CHD with DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Cognitive subscale		
Median	60 [55 – 90]	95 [55 – 130]
Mean and SD	65 (±10.5)	91.5 (±16.5)
Language subscale		
Median	75.5 [62 - 112]	94 [65 – 115]
Mean and SD	78.2 (±15.2)	94.5 (±11.3)
Motor subscale		
Median	58 [46 - 88]	86.5 [58 – 112]
Mean and SD	61 (±14.1)	85.7 (±13.8)
Three-months post-cardiac intervention	**(n=5)**	**(n=20)**
Cognitive subscale		
Median	55 [55 – 70]	90 [55 -105]
Mean and SD	60 (±7.1)	90.8 (±12.7)
Language subscale		
Median	71 [50 – 83]	92.5 [71 – 112]
Mean and SD	69.2 (±12.1)	93.2 (±13.1)
Motor subscale		
Median	46 [46 -73]	91 [46 – 112]
Mean and SD	55 (±12.7)	89.3 (±14.7)
Six-months post-cardiac intervention	**(n=5)**	**(n=17)**
Cognitive subscale		
Median	55 [55 – 65]	90 [55 -100]
Mean and SD	58 (±4.5)	90.9 (±13.3)
Language subscale		
Median	65 [57 – 79]	91 [65 – 109]
Mean and SD	66.2 (±6.9)	88.8 (±13.5)
Motor subscale		
Median	55 [49 – 70]	97 [49 -121]
Mean and SD	57.4 (±8.3)	92.3 (±18.9)

* Scores < 70 = delayed, 70-84 at risk and >85 normal

Mean scores for all three of the sub-categories of the BSID-III were below the mean score of 100 in both groups at all three time-points of assessment. The mean scores for all the subscales in the group of CHD without DS were all within 1SD of the mean at all assessment time points. The scores on all of the subscales for the group with CHD with DS were considerably lower than the group with CHD without DS at all three time points of assessment.

At baseline, 90% of the participants in the group of CHD with DS were at risk of, or had delayed motor development, compared to only 40% in the CHD without DS group. By six-month post-cardiac intervention risk of, and delays in motor development in the group of CHD without DS had declined to 29.4%. Where motor delays were present in this group they were mild or moderate in nature. In contrast, by six-month post-cardiac intervention 100% of the children in the CHD with DS group were at risk of, or presented with delayed motor development. Where motor delays were present in this group the majority (60%) were severe in nature.

At baseline, 90% of the participants in the group of CHD with DS were at risk of, or presented with delayed cognitive development, compared to only 27% in the CHD without DS groups. By six-month post-cardiac intervention risk of, and delayed cognitive development had declined in the group of CHD without DS to 17.2%. In contrast, by six-month post-cardiac intervention 100% of participants in the group of CHD with DS were at risk of, or presented with delayed cognitive development.

At baseline, 80% of the participants in the group of CHD with DS were at risk of, or presented delayed language development, compared to only 13.3% in the CHD without DS group. By six-month post-cardiac intervention risk of, and delayed cognitive development had increased in the group of CHD without DS group to 47.2% and to 100% in the CHD with DS group.

Developmental outcomes were therefore to be considered considerably poorer for participants with CHD who had DS, when compared to those without DS across all areas of development both before and after cardiac intervention.

Hypotonia was marked in all participants (100%) in the group of CHD with DS both before and after cardiac intervention. Hypotonia was present in 26.7% of participants in the CHD without DS group before cardiac intervention and tended to resolve over time.

5.13.1.6 Parents' perception of health related quality of life

Parents' perception of their children's HRQOL reflected as a total score out of a 100 is presented in Table 5.32. Values indicated are medians with ranges and means with standard deviations.

Table 5.32 Perceived health-related quality of life outcomes of children with CHD with DS compared to those with CHD without DS

PedsQL™ total score	CHD with DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Median (range)	77.5 [63.9 – 88.2]	81.3 [48.6 – 97.2]
Mean and SD	75.5 (±8.1)	78.4 (±13.6)
Three-month post-cardiac intervention	**(n=5)**	**(n=20)**
Median (range)	77.8 [29.2 – 93.3]	90.3 [64.4 – 100]
Mean and SD	69.7 (±29.8)	87.9 (±11.2)
Six-month post-cardiac intervention	**(n=5)**	**(n=17)**
Median (range)	76.1 [74.4 -79.4]	89.5 [52.2 – 100]
Mean and SD	76.5 (±2.1)	87.3 (±11.3)

Parents in both groups perceived their children's HRQOL as good at all time points of assessment over the study. However, parents of participants in the group of CHD with DS viewed their children as having a poorer HRQOL than those of children with CHD without DS both before and after cardiac intervention. Parents of children with CHD without DS were of the view that their children's HRQOL improved to a greater extent post-cardiac intervention than those parents of children with CHD with DS.

5.13.1.7 Parenting stress outcomes

Parenting stress outcomes, reflected as a percentile score, are presented in Table 5.33. Values reported are medians with ranges and means with standard deviations.

Table 5.33 Levels of parenting stress in children with CHD with DS compared to those with CHD without DS

Subscales of the PSI-SF	CHD with DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Parenting distress		
Median (range)	87.5 [35 – 99]	90 [10 – 99]
Mean and SD	74.4 (±24.9)	86.4 (±17.3)
Parent-child dysfunction		
Median (mean)	95 [40 – 99]	80 [40 – 99]
Mean and SD	86.7 (±19.2)	77.8 (±19.8)
Difficult child		
Median (range)	75 [25 – 95]	77.5 [1 – 99]
Mean and SD	73 (±20.8)	65.2 (±27.9)
Total stress		
Median (range)	92.5 [40 – 99]	90 [5 - 99]
Mean and SD	82.4 (±20.9)	84.3 (±18.9)

Subscales of the PSI-SF	CHD with DS	CHD without DS
Three-months post-cardiac intervention	**(n=5)**	**(n=20)**
Parenting distress		
Median (range)	80 [30 – 95]	75 [1 – 95]
Mean and SD	68 (±30.9)	62.8 (±32.9)
Parent-child dysfunction		
Median (range)	95 [85 - 99]	70 [5 – 99]
Mean and SD	(93.6 (±6.1)	67 (±27.9)
Difficult child		
Median (range)	75 [50 - 95]	52.5 [1 – 95]
Mean and SD	75 (±18.4)	47.1 (±26.9)
Total stress		
Median (range)	90 [60 - 99]	77.5 [1 – 99]
Mean and SD	84.6 (±16.9)	65.1 (±29.8)

Subscales of the PSI-SF	CHD with DS	CHD without DS
Six-months post-cardiac intervention	**(n=5)**	**(n=17)**
Parenting distress		
Median (range)	65 [35 – 95]	65 [1 – 95]
Mean and SD	62 (±24.9)	56.5 (±34.3)
Parent-child dysfunction		
Median (range)	95 [80 – 99]	55 [5 – 97]
Mean and SD	91 (±7.3)	55.1 (±34.6)
Difficult child		
Median (range)	80 [35 – 99]	40 [1 – 90]
Mean and SD	(76.8 (±24.7)	39.1 (±34)
Total stress		
Median (range)	80 [55 – 99]	50 [1 – 95]
Mean and SD	81.8 (±17.3)	50.8 (±35.8)

Before cardiac intervention, parents of participants with CHD with DS felt that their children did not live up to their expectations to a greater extent than those with CHD without DS. Stress experienced by parents in both groups was comparable prior cardiac intervention. The majority of parents in both groups experienced clinically significant levels of stress (stress scores above the 90th percentile considered to be clinically significant) before their children underwent cardiac intervention.

At both three-months and six-months post-cardiac intervention, parents of participants with CHD with DS felt that their children did not live up to their expectations to a greater extent, and were more difficult to parent, than children without DS. At both three-and six-month post-cardiac intervention the stress experienced by parents in their parenting role was far greater for the parents of children with CHD with DS.

5.13.2 Outcomes for cyanotic versus acyanotic heart defects

The majority (80%) of the participants in this study were diagnosed with acyanotic heart defects. Differences in key outcomes of participants with cyanotic heart defects compared to acyanotic heart defects will be presented in the following section. The proportion of this sample with cyanotic heart defects is shown in Figure 5.10.

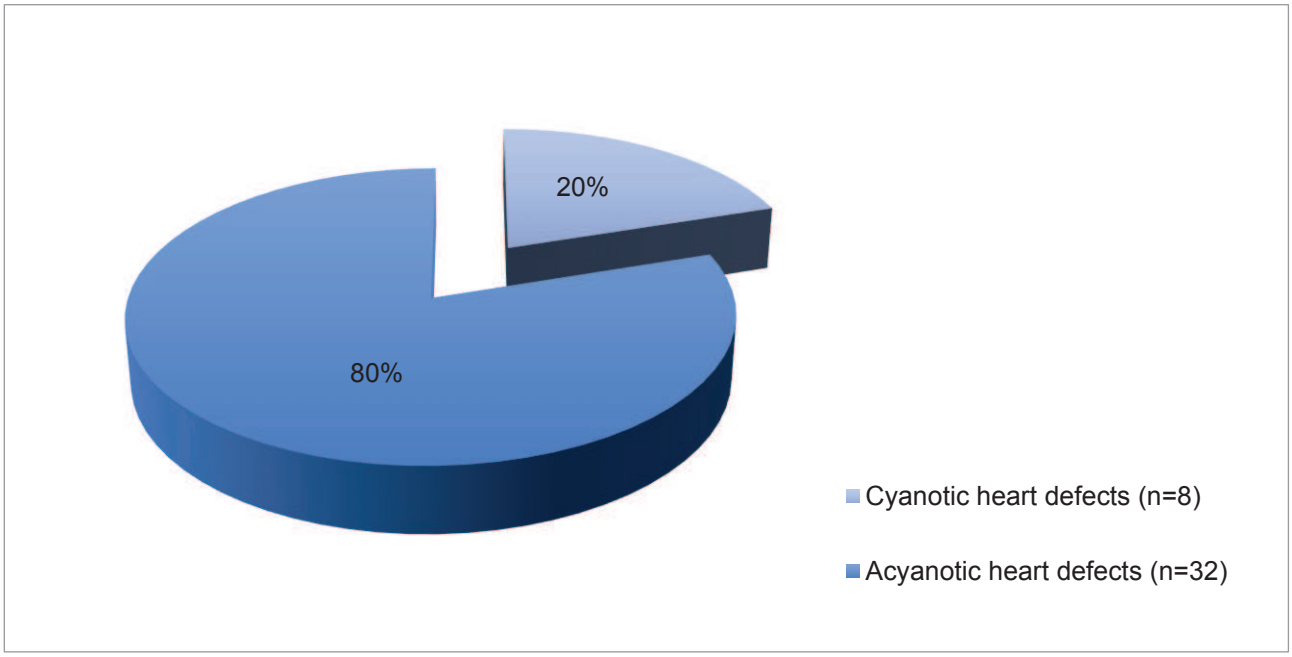

Figure 5.10 Prevalence of cyanotic heart defects in this study sample (n=40)

5.13.2.1 Sociodemographic information

Sociodemographic information was similar for both the cyanotic and acyanotic groups.

5.13.2.2 Cardiology diagnostic information

The mean cardiac disease severity in the cyanotic heart defect group was moderate to severe, while the mean severity in acyanotic group was moderate. The children in the cyanotic group tended to have more severe CHD than the acyanotic group.

The most prevalent congenital heart defect in the cyanotic group was DORVs (30%), whilst VSDs (50%) were the most common defect in the acyanotic group.

5.13.2.3 Surgical intervention and post-operative medical course

Those participants with cyanotic heart defects in the current study underwent their first cardiac surgery at a slightly younger age than those participants with acyanotic heart defects.

The duration of CPB tended to be longer in the case of children with cyanotic heart defects compared to acyanotic heart defects, but the aorta cross-clamp times were similar for both groups. The cardiothoracic ICU length of stay and hospital length of stay post-surgery tended to be slightly longer for children with cyanotic heart defects.

5.13.2.4 Growth outcomes

Anthropometric data using the z-score system for weight-for-age, height-for-age and head circumference-for-age at baseline and for the three-month and six month post-cardiac intervention are presented in Table 5.34. Values reported are reported as medians and means with standard deviations.

Table 5.34 Growth outcomes for children with cyanotic heart defects compared to those with acyanotic heart defects

Growth parameter	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Weight for age z-score		
Median	-2.8	-2.6
Mean and SD	-2.5 (±1.4)	-2.5 (±1.5)
Height for age z-score		
Median	-2.5	-1.6
Mean and SD	-3.3 (±2.8)	-1.9 (±2.3)
Head circumference for age z-score		
Median	-1.4	-1.4
Mean and SD	-1.5 (±2.2)	-1.3 (±1.4)
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Weight for age z-score		
Median	-2.9	-1.7
Mean and SD	-3.0 (±0.8)	-1.6 (±1.7)
Height for age z-score		
Median	-1.0	-1.2
Mean and SD	-1.2 (±1.6)	-1.6 (±1.9)
Head circumference for age z-score		
Median	0.3	-1.2
Mean and SD	0.2 (±1.7)	-1.1 (±1.7)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Weight for age z-score		
Median	-2.2	-1.8
Mean and SD	-1.8 (±2.5)	-1.6 (±1.7)
Height for age z-score		
Median	-1.8	-1.6
Mean and SD	-1.7 (±1.8)	-1.8 (±1.6)
Head circumference for age z-score		
Median	0.3	-0.6
Mean and SD	0.5 (±1.3)	-0.5 (±1.9)

The majority of the participants in both groups (65.6% and higher) had suboptimal growth prior to cardiac intervention. A higher percentage of children in the cyanotic group had malnutrition (75%) and stunting (62.5%), and the extent of the growth failure in this group

tended to be greater prior to cardiac intervention. The prevalence of microcephaly was found to be high in both groups.

Growth across all growth parameters improved in both groups post-cardiac intervention, and growth trends tended to be comparable by six-month post-cardiac intervention. However, the weight catch-up post-cardiac intervention tended to be slower in children in the cyanotic group.

5.13.2.5 Neurodevelopmental outcomes

Composite scores for cognitive, language and motor subscales of the BSID-III for both groups are reported in Table 5.35 (See table on the following page). Values indicated are medians with ranges and means with standard deviations.

Table 5.35 Developmental outcomes on the BSID-III for children with cyanotic heart defects compared to those with acyanotic heart defects

Variable	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Cognitive sub-scale		
Median (range)	92.5 [55 – 105]	85 [55 – 130]
Mean and SD	89.4 (±17)	83.8 (±19.6)
Language sub-scale		
Median (range)	100 [65 – 112]	91 [62 – 115]
Mean and SD	93.9 (±17.5)	89.6 (±13.3)
Motor sub-scale		
Median (range)	85 [46 – 112]	82 [49 – 110]
Mean and SD	82.8 (±18.8)	78.7 (±17.3)
Three-month post cardiac intervention	**(n=4)**	**(n=21)**
Cognitive sub-scale		
Median (range)	90 [85 – 95]	90 [55 – 105]
Mean and SD	90 (±4.1)	83.6 (±18.5)
Language sub-scale		
Median (range)	106 [91 – 109]	83 [50 – 112]
Mean and SD	103 (±8.5)	85.6 (±15.7)
Motor sub-scale		
Median (range)	85 [82 – 94]	91 [46 – 112]
Mean and SD	86.5 (±5.7)	81.6 (±21.5)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Cognitive sub-scale		
Median (range)	95 [80 – 110]	87.5 [55 – 110]
Mean and SD	95 (±12.2)	80.8 (±18.7)
Language sub-scale		
Median (range)	90 [65 – 103]	81 [59- 109]
Mean and SD	87 (±17.9)	82.6 (±15.4)
Motor sub-scale		
Median (range)	89.5 [73 – 121]	89.5 [49 – 121]
Mean and SD	93.3 (±21.8)	82.3 (±22.8)

* score < 70 = delayed, 70-84 at risk and >85 normal, >85 normal

Developmental performance across all the subscales of the BSID-III (cognitive, language and motor) tended to be similar at all time points of assessment, both before and after cardiac intervention, when the BSID-III score ranges of the participants were compared.

5.13.2.6 Parents' perception of health-related quality of life

Perceived HRQOL as reflected as a total score out of 100 is reflected in Table 5.35. Values indicated are medians with ranges and means with standard deviations.

The perceived HRQOL outcomes for children with cyanotic and acyanotic heart defects are presented in Table 5.36.

Table 5.36 Perceived health-related quality of life outcomes for children with cyanotic heart defects compared to acyanotic heart defects

PedsQL™ total score	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Median (range) Mean and SD	79.5 [48.6 – 93.3] 75 (±16.2)	81 [49.3 – 97.2] 78.3 (±11.5)
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Median (range) Mean and SD	91.7 [88.9 – 99.3] 92.9 (±4.6)	88.2 [29.9 – 100] 84.3 (±17)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Median (range) Mean and SD	87.9 [84.8 – 90] 87.6 (±2.3)	86.4 [52.2 – 100] 84.6 (±11.9)

HRQOL was good in both groups at all assessment time points. Perceived HRQOL was similar in both groups at all assessment time points both before and after cardiac surgery. Parents in both groups perceived their children's HRQOL to have improved post-cardiac intervention.

5.13.2.7 Parenting stress outcomes

Levels of parenting stress reflected as a percentile are presented in Table 5.37. Values reported are medians with ranges and means with standard deviations.

Table 5.37 Levels of parenting stress for children with cyanotic heart defects compared to acyanotic heart defects

Sub-scales of the PSI-SF	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Total stress		
Median (range)	80 [50 -99]	90 [5 – 99]
Mean and SD	78.5 (±19.1)	85.2 (±19.3)

Sub-scales of the PSI-SF	Cyanotic	Acyanotic
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Total stress		
Median (range)	75 [15-80]	80 [1 – 99]
Mean and SD	61.3 (±31)	70.5 (±28.6)

Sub-scales of the PSI-SF	Cyanotic	Acyanotic
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Total stress		
Median (range)	25 [5 - 90]	72.5 [1-99]
Mean and SD	36.3 (±37.1)	62.6 (±33.4)

A high number of the parents (37.5% and higher) in both groups experienced clinically significant levels of stress (total stress score higher than the 90th percentile) before their child underwent cardiac intervention. Parenting stress declined in both groups after cardiac intervention and over time. Levels of parenting stress tended to be similar in both groups at all three of the time-points of assessment when the PSI-SF total score ranges of the participants were compared.

5.14 Summary

The majority of participants in this study were diagnosed with acyanotic heart defects, and in most cases, the disease severity was moderate. A quarter of the participants presented with genetic comorbidity in the form of DS. The majority of participants had at least one hospital admission prior to cardiac intervention, mostly for respiratory-related complications. Most underwent open-heart surgery in infancy and were placed on CPB. Most children had an uncomplicated medical course post-cardiac surgery. The mortality rate was 15%, which contributed to the loss to follow-up of 47.5% over the course of this study.

The majority of families had to travel distances of greater than 100 km to access cardiac services. Both mothers and fathers had low levels of education and most families were from a low socioeconomic class.

The findings of this study confirm that young children with CHD are at risk of developmental delay across all areas of development as measured by the BSID-III. Younger children initially showed the greatest risk of, and delays in motor development followed by cognitive development. Language delays became more prevalent with increasing age and with increasing skill complexity. In the most cases developmental delays were mild to moderate in severity. However, there were no significant changes in developmental outcome over time and post-cardiac intervention. Children with CHD with DS had worse developmental outcomes across all areas of development compared to children without DS, whilst the developmental outcome in children with cyanotic and acyanotic heart defects was found to be similar. Variables most strongly associated with developmental outcomes included the presence of DS and maternal age. Other variables found to be associated with developmental outcome include age at first surgery and disease severity.

Hypotonia was the most significant abnormal finding on neurological examination, and was marked in all participants with DS. Hypotonia resolved in participants with CHD without DS over time.

The majority of the participants had suboptimal growth prior to cardiac intervention. A quarter of the participants also presented with microcephaly related to their growth failure. Growth

(weight and head circumference) improved significantly over time and post-cardiac intervention. The growth trends of children with CHD with DS were similar to those with CHD without DS. Growth in children with cyanotic heart defects tended to be poorer than those with acyanotic heart defects both before and after cardiac intervention.

Parents perceived their children's HRQOL as good at all assessment time points. However, parents' perception of their children's HRQOL improved significantly post-cardiac intervention. Perceived HRQOL was similar in participants with cyanotic and acyanotic heart defects. Parents of children with CHD with DS perceived their children's HRQOL as poorer than those with CHD without DS. The variables that were associated with parental perception of their child's HRQOL prior to cardiac intervention included motor developmental performance and levels of parenting stress. No variables were found to be significantly associated with HRQOL outcomes at either three-month or six-month post-cardiac intervention.

The majority of parents experienced clinically significant levels of stress in their parenting role prior to cardiac intervention. More than half of the caregivers felt that their child failed to meet their expectations. Levels of parenting stress declined significantly post-cardiac intervention and over time. Although dysfunction in the parent-child interaction improved after cardiac intervention, this continued to be the aspect that contributed most to parenting stress. Parents of children with cyanotic and acyanotic heart defects experienced similar levels of stress. However, parents of children with CHD with DS tended to continue to experienced higher levels of stress than parents of children with CHD without DS after cardiac intervention. They found that their children failed to live up to their expectations to a greater extent than those with children with CHD without DS after cardiac intervention. Variables associated with levels of parenting stress included language developmental performance, perceived HRQOL, age of the child at first cardiac surgery and maternal age. Parents' perception of their child's HRQOL and parenting stress levels were found to be closely interlinked, especially prior to cardiac intervention.

The findings will be discussed in more detail and in the context of the published literature in Chapter six.

CHAPTER 6

DISCUSSION

The results of this study will be discussed in more detail in this chapter. A discussion of the sample size and study attrition will be presented. The sociodemographic, diagnostic cardiology and surgical management information will also be discussed.

Each of the main outcomes that were assessed will be discussed in the context of the available research, and where indicated, possible reasons for the outcomes and changes seen over time will be provided. The most important outcomes for subgroups will be discussed briefly. These are to include the outcomes for children with CHD with DS and those with cyanotic heart defects.

The strengths of the study and challenges faced during this study, as well as the limitations, will be discussed. A number of recommendations for clinical management and future research will be presented.

6.1 Recruitment, sample size and study attrition

Recruiting participants into this study posed a challenge at the outset, in part due to the fact that cardiac neurodevelopmental follow-up did not form part of standard cardiac care offered at the Universitas Academic Hospital Cardiac Unit. This is not a problem unique to cardiac clinical practice in SA. Despite routine cardiac neurodevelopmental follow-up being recommended as part of standard cardiac clinical care in the AHA guidelines (Marino et al., 2012), most cardiac centres in developed countries fail to assess neurodevelopment routinely as part of standard cardiac care (Brosig Soto et al., 2011). Long et al. (2015) and Kendall et al. (2003) similarly reported that cardiac neurodevelopmental follow-up did not

form part of routine cardiac care in either Australia or the UK respectively. To date longitudinal neurodevelopmental follow-up in children with CHD in developed countries has mostly been done in the context of clinical cardiac outcome-based research (Brosig Soto et al., 2011).

The fact that cardiac neurodevelopmental follow-up did not form part of standard cardiac care at the Universitas Academic Hospital Cardiac Unit resulted in challenges in establishing referral and recruitment systems for this study. Medical and nursing personnel in both the Cardiology Department and Cardiothoracic Department were unfamiliar with the processes involved in performing neurodevelopmental assessment as part of patients' standard care. Putting systems in place to access the surgery lists in advance to identify potential participants for inclusion and allowing for sufficient time for recruitment and baseline assessment took time. Integrating neurodevelopmental follow-up into routine clinical care, both in the ward and busy outpatient clinic setting posed several logistical and time-related challenges. Referral systems became more established over time and recruitment into the study became easier as collaborative working relationships were established with medical and nursing personnel.

Challenges in establishing referral and recruitment systems in a clinical setting where cardiac neurodevelopmental follow-up is not well established and does not form part of standard cardiac care are not unique to this study. Brosig Soto et al. (2011) reported similar challenges in their study done in the US as did Long et al. (2015) in their early developmental intervention study done in Australia.

A further challenge in recruiting participants into this study was that all participants had to undergo a mandatory comprehensive neurodevelopmental assessment on the BSID-III prior to cardiac intervention. Only two neurodevelopmental follow-up studies by Majnemer et al. (2009) and Dittrich et al. (2003) have reported including a neurodevelopmental assessment prior to cardiac intervention in their research protocols. Their developmental assessments were similarly conducted on the day prior to cardiac surgery. Only Majnemer et al. (2009) mandated neurodevelopmental assessment prior to surgery. Dittrich et al. (2003) on the other hand, reported only being able to perform neurodevelopmental assessment on 68.7% of their participants prior to cardiac intervention.

Mandating a baseline neurodevelopmental assessment resulted in the exclusion of medically unstable and critically ill children and those children having to undergo emergency cardiac surgery. This in effect limited the sample size to some extent. Majnemer et al. (2009) and Dittrich et al. (2003) also noted similar participant exclusions from their pre-operative assessments.

This aforementioned factor may also have resulted in an under-representation of children with more severe cardiac defects in the current study sample, as the children who were medically unstable or required emergency surgery were most likely to have been those children with more severe forms of CHD.

More recently published studies where multiple neurodevelopmental assessments took place only assessed participants' neurodevelopmental status after cardiac intervention (Medoff-Cooper et al., 2016; Mussatto et al., 2015; Mussatto et al., 2014; Chock et al., 2012; Long et al., 2012a; Sananes et al., 2012; and Joynt et al., 2009). Furthermore, the AHA guidelines fail to provide clarity on developmental assessment during infancy in relation to cardiac intervention (Marino et al., 2012).

Gaynor et al. (2015) noted that one of the greatest challenges facing cardiac neurodevelopmental follow-up studies is that they are limited by small sample sizes and that they are usually single centre-based. Even though the sample size in the current study was small at 40 participants, recruited over a 17-month period, the participant numbers are still comparable with those reported in other neurodevelopmental outcome studies conducted at major cardiac centres in developed countries when sample sizes are broken down into the average number of participants recruited per annum. Recent cardiac neurodevelopmental outcome studies using the BSID-III as the outcome measure recruited between 16 and 32 participants per annum (Mussatto et al., 2015; Mussatto et al., 2014; Beca et al., 2013; Long et al., 2012a; Acton et al., 2011; Brosig Soto et al., 2011).

The attrition rate in the current study was high at 47.5%, yet it remained comparable with the rates reported in the literature. Gaynor et al. (2015) highlighted the fact that longitudinal cardiac clinical follow-up studies are challenged by loss to follow-up. The reported loss to follow-up in multiple assessment neurodevelopmental follow-up studies in the developed

world varies considerably. Long et al. (2015) reported a loss to follow-up of 44%. Hoskoppel et al. (2010) reported a loss to follow-up of 35% at their second follow-up visit, which escalated to 64% by their third follow-up visit. Chock et al. (2012) reported a loss to follow-up of 43% over the duration of their study.

Despite patients surviving and recovering from cardiac surgery, many require long-term follow-up, but adherence with cardiac follow-up has been found to be poor in Africa (Tantchou Tchoumi et al., 2011) and in SA (Van Deventer et al., 2015; Lee, 2014). Lee (2014) reported a 28.8% loss to follow-up in their study of cardiac patients conducted in Cape Town, SA; whilst Van Deventer et al. (2015) reported that the loss to follow-up at a tertiary cardiac unit in the Western Cape province of SA was 44%. In a study of cardiac patients in Cameroon, Tantchou Tchoumi et al. (2011) reported an early loss to follow-up of 32%, and a late loss to follow-up of 40%.

In the current study, the attendance rate of follow-up visits at three-month post-cardiac intervention was 62.5%, which declined to 55% by the time of the six-month post-cardiac intervention follow-up. Loss to follow-up was found to increase over time despite families being reminded of follow-up appointments and being remunerated for their travelling expenses. A possible reason for the decline in participation over time in this study could have been that the six-month follow-up did not always coincide with a routine cardiology follow-up appointment. This meant that the attendance of the six-month post-cardiac intervention neurodevelopmental follow-up on its own required a special effort on the part of the families. Both Hoskoppel et al. (2010) and Tantchou Tchoumi et al. (2011) noted a similar decline in adherence with follow-up appointments over time. Tantchou Tchoumi et al. (2011) suggested that poverty and the distance that had to be travelled by families to access cardiac services discouraged compliance with follow-up appointments. Hoskoppel et al. (2010) failed to provide reasons for their loss to follow-up over time.

Reasons for loss to follow-up in the current study were found to be multiple. Mortality contributed to study attrition. The mortality rate in the current study was 15%. This aligns with the survival rate of 85% for children with CHD reported in current literature (Marino et al., 2012; *The Lancet*, 2012; Hoosen et al., 2010b).

Other factors contributed to the loss to follow-up including distance to be travelled to access cardiac services, unreliable inter-hospital transport services, financial difficulties on the part of families and a lack of understanding of primary caregivers of the importance of neurodevelopmental follow-up.

The majority (65%) of the participants in the current study lived more than 100 kilometres from the cardiac service point. Long et al. (2015), Steiber et al. (2012) and Kendall et al. (2003) all identified that geographical constraints posed a significant challenge to the provision of cardiac services post-cardiac intervention in developed countries. These authors further suggested that the distance to be travelled to follow-up needed to be considered a potential limitation to the implementation of cardiac neurodevelopmental programmes, as well as EI programmes. Brosig et al. (2014) and Brosig Soto et al. (2011) agreed, that families who lived a considerable distance from the cardiac service point often failed to participate in cardiac neurodevelopmental follow-up.

Most families (87.5%) in this study had a low SES, and the costs of travel, as well as parents who were employed not wanting to miss work due to the potential loss of income, and availability of inter-hospital transport affected adherence to follow-up appointments. Van Deventer et al. (2015), Lee (2014), Amakali and Small (2013), Mocumbi et al. (2011) and Tantchou Tchoumi et al. (2011) all similarly found that the costs and time associated with cardiac follow-up deterred families from complying with follow-up appointments. Lee (2014) reported that in a study done in Cape Town, one-third of the patients lost to cardiac follow-up resided in distant provinces in SA or in neighbouring countries. Furthermore, Amakali and Small (2013) noted that a lack of access to inter-hospital transport made the facilitation of follow-up cardiac care difficult in resource-poor settings.

Anecdotally, most parents' knowledge and understanding of the importance of cardiac neurodevelopmental follow-up was found to be lacking in the current study. The reason for this could be that cardiac neurodevelopmental follow-up did not form part of routine cardiac care, and that parents were not provided with adequate information on the risk CHD poses to their child's developmental outcome (this will be addressed in Chapter seven through the development of the family information document and home-based developmental activity programme). Mocumbi et al. (2011) and Van Deventer et al. (2015) both commented on the

fact that families knowledge and understanding of their child's health condition influenced adherence to follow-up. Brosig Soto et al. (2011) and Long et al. (2015) suggested that the decline in post-operative compliance with neurodevelopmental follow-up could be as a result of parents feeling that their child was "doing well", or that the child was seeing a rehabilitation therapist closer to home (Brosig Soto et al., 2011). Long et al. (2015) also reported parents not attending follow-up as they felt it was "unnecessary". Brosig et al. (2014) were of the opinion that getting the buy-in and commitment of parents to comply with follow-up was critical to the success of cardiac neurodevelopment follow-up.

Ten percent of participants were lost to follow-up as they became untraceable, and could no longer be contacted via cellular phone at the number provided. Van der Meer and Loock (2008) similarly found that the limited methods of distance communication available to most South Africans, such as telephone and e-mail services, was an important reason why patients were lost to medical follow-up. Ninety percent of South Africans make use of cellular phones for communication, with SMS text messaging being the most common form of cellular phone use in Africa (Pew Research Centre, 2015). There are still challenges with cellular phone communication in Africa as most cellular phone owners are on "pay as you go" and frequently change phones and phone numbers. In addition, unreliable network coverage, the cost of charging cellular phones, and the purchasing of airtime are still considerable hurdles for families with financial constraints, and those residing in rural areas (Dobush, 2015).

Confirming follow-up appointments via telephone appears to be problematic not only in developing countries. Brosig Soto et al. (2011) also reported that 17% of their study participants in the US did not respond to telephone calls and were subsequently lost to follow-up.

6.2 Sociodemographic information

The majority of children in the current study were female. Consecutive sampling and the relatively small sample size may have contributed to the coincidental gender profile. Okoromah et al. (2011) noted the ratio of males to females born with CHD as being 1.4:1. In most other comparable neurodevelopmental outcome studies, males were found to be in

the slight majority (Medoff-Cooper et al., 2016; Brosig Soto et al., 2011; Beca et al., 2013; Mussatto et al., 2014; Acton et al., 2011; Long et al., 2012a).

The results of the current study indicated that 22.5% of the children were born prematurely and 25% had a low birth weight. Goff et al. (2011) reported that approximately 15% of children with CHD are born either prematurely and/or with a low birth weight. The higher prevalence of low birth weight in the current study population could possibly be attributed to the low SES of the families and the gestational age of the child (Kader and Perera, 2014; Taylor and Sarathchandra, 2014). The low birth weight of children in this study could also be the result of growth being restricted in utero due to the abnormal foetal blood flow caused by the heart defect (Roman, 2011; Knirsch et al., 2010).

The average gestational age of participants was 38 weeks, with a range of 31 to 41 weeks. This compares favourably with the average gestational age reported in other outcome studies (Gaynor et al., 2015; Mussatto et al., 2014; Beca et al., 2013; Chock et al., 2012; Goff et al., 2011; Simons et al., 2010).

The mean birth weight in this study was 2878.5 grams. The average birth weights in Knirsch et al. (2010), Matsuzaki et al. (2010) and Simons et al.'s (2010) studies were under 3000 grams. However, most of the studies report an average birth weight ranging between 3000 and 3500 grams (Gaynor et al., 2015; Schaefer et al., 2013; Beca et al., 2013; Chock et al., 2012; Goff et al., 2011; Bellinger et al., 2009).

The inclusion of premature infants in neurodevelopmental outcome studies is variable. Prematurity was considered an exclusion criterion in some studies, whilst other studies included children irrespective of gestational age. Both Mussatto et al. (2014) and Brosig Soto et al. (2011) reported that 20% of the participants in their respective studies were born prematurely. Exclusion of premature infants from some studies may be the result of prematurity being considered an independent risk factor for developmental delay (McGowan et al., 2011).

The median age of the mothers in this study was 30 years, but ranged from 16 to 43 years. The median age of mothers in SA at the age of the birth of their first child is 22.5 years

(Statistics South Africa, 2012). There were a large number of mothers over the age of 30 years, in particular the mothers of children with CHD with DS in this study were found to be older with a median age of 37 years.

The level of education for mothers and fathers in this study was low, averaging grade nine to 11. According to the General Household Survey (2014), only 28.7% of South African's have attained grade 12 as their highest level of education (Statistics South Africa, 2015). In the South African context, black African women are at a disadvantage with regards to educational opportunities (Statistics South Africa, 2013). This is in stark contrast with the educational attainment of parents reported in outcome studies from developed countries, where the level of parental education at a minimum was a high school graduate, with many parents reporting some level of tertiary education (Gaynor et al., 2015; Mussatto et al., 2015; Acton et al., 2011).

Consistent with the population served by the Universitas Academic Hospital Cardiac Unit, the majority of the participants' ethnicity was black African (75%), followed by mixed race (22.5%), and then white (2.5%). The ethnic profile of this study differed from other outcome-based studies, where the majority of the participants were white. It is important to be cognisant of the fact that most of these studies were done in North America and Europe. Looking at the study with the largest reported sample of 1770 participants from 22 institutions, Gaynor et al. (2015) reported that 84% of the cohort in their study was white. This would make this the first study where the majority of the sample consisted of black African children.

The majority of the parents in this study were from a low socioeconomic class. To the contrary, most families represented in CHD outcome-based research done in developed countries were from a middle socioeconomic class (Mussatto et al., 2014; Brosig Soto et al., 2011; Acton et al., 2011). Low levels of education and high rates of unemployment amongst parents contributed to the low SES of the families in this sample. In most instances, the fathers were the primary breadwinners; however, only 52% reported having full-time employment. The employment rate is reflective of the South African economic climate where the unemployment rate is high. In 2015, it was reported that 26.4% of potentially economically active South Africans were unemployed (ENCA, 2015).

The majority of the caregivers were mothers and most did not work outside the home. The unemployment rate amongst women in SA remains higher than that of men (Statistics South Africa, 2013), which was similar to the findings in the current study. Additional factors that may have contributed to the women in this study not working outside of the home may be the burden of caring for a child with a chronic health condition.

6.3 Congenital heart disease profile

The profile of the type of CHD, based on the presence or absence of cyanosis in this study, was comparable to that reported in the literature (Hanson, 2015; Starr and Tucker, 2005). Acyanotic heart defects were diagnosed in 80% of the participants, with cyanotic heart defects present in 20% of the participants. There may have been a slight under-representation of cyanotic heart defects in this study due to the fact that critically ill children and those requiring emergency surgery were excluded. These children were more likely to have had cyanotic heart defects.

The profile of congenital heart defects in this study sample was comparable to that reported in the literature. The most common acyanotic defects reported in the current study sample were VSDs, followed by AVSDs and then PDAs (Hanson, 2015; Nousi and Christou, 2010). Similarly, the most common cyanotic defects were DORVs and TGAs, followed by TOFs (Hanson, 2015; Nousi and Christou, 2010).

The majority of the participants in this study had moderate or moderate to severe CHD. Yildiz et al. (2009), who applied the same severity classification system in their study, also reported that the majority of the participants in their study had disease of moderate severity. However, the current study reported far fewer cases of mild CHD, at only 2.5%, compared to the 36.1% reported by Yildiz et al. (2009). In addition, the current study also reported far fewer cases of severe CHD at only 2.5%, compared to the 8.1% reported by Yildiz et al. (2009).

The low number of children presenting with mild CHD in the current study could be explained by the lack of neonatal screening and missed diagnoses in the case of asymptomatic CHD in SA as a result of service delivery failures and an overburdened public health system

(Brown, 2014; Hoosen et al., 2010a; Hoosen et al., 2010b). In addition, cardiac defects may have gone undiagnosed as a result of poverty and low socio-economic status limiting access of families to specialist healthcare services (Ataguba et al., 2011), resulting in a large number of children with CHD in SA not being diagnosed (Reuters South Africa, 2015).

The low number of children with severe CHD represented in this study could be attributed to critically ill and medically unstable children and those requiring emergency surgery being excluded. These children would most likely have been those with more severe forms of CHD (Gaynor et al., 2015). In addition, children with the severest forms of CHD such as HLHS often do not survive long enough in SA to undergo palliation (Brown, 2016).

Twenty-five percent of the participants in this study were diagnosed with a genetic comorbidity. In all cases, the genetic abnormality diagnosed was DS. Neurodevelopmental outcome studies that included children with genetic comorbidity reported that between 8.7 and 22% of study participants were diagnosed with a genetic abnormality or syndrome (Gaynor et al. 2015; Goff et al., 2011; Brosig Soto et al., 2011).

6.4 Surgical intervention and post-operative medical course

The majority of the participants in this study underwent cardiac surgery in infancy. The median age at first surgery was 7.5 months with a mean age of 9.4 (±5.5) months. Most children included in neurodevelopmental outcome research underwent their first cardiac surgery in early infancy (Gaynor et al., 2015; Mussatto et al., 2015; Mussatto et al., 2014; Beca et al., 2013; Long et al., 2012a; Sananes et al., 2012; Brosig Soto et al., 2011; Bellinger et al., 2009; Joynt et al., 2009; Majnemer et al., 2009). However, there were isolated studies that included participants where the age at first cardiac surgery was over one year (Schaefer et al., 2013; Von Rhein et al., 2011; Simons et al., 2010).

The age at first cardiac intervention in this study was older than reported in the majority of the outcome studies. Older age at the time of first cardiac surgery could be attributed to delayed diagnosis of the child's CHD. Many children in this study lived in rural areas and may not have had access to specialist care. In addition, bottlenecks in the referral system and problematic inter-hospital transport services within the public health sector may have

resulted in delayed access to care (Van Deventer et al., 2015; Lee, 2014; Robertson, 2006). Overburdened cardiac services may also have resulted in children requiring elective surgical intervention having to wait for surgery (Hoosen et al., 2010a; Hoosen et al., 2010b). As discussed previously, neonates, critically ill children and those requiring emergency surgery were excluded from this study. This could also have contributed to the older age of included children at the time of first cardiac surgery in this study.

The majority of the participants in this study underwent open-heart surgery with CPB. The median duration of CPB in this study was 104 minutes and an average duration of 111.8 minutes. Considerable variation in CPB time is reported in the literature. Reported median CPB duration ranged from 49 minutes to 215 minutes (Mussatto et al., 2015; Mussatto et al., 2014; Long et al., 2012a; Von Rhein et al., 2012; Goff et al., 2011; Brosig Soto et al., 2011; Joynt et al., 2009); whilst the reported average CPB duration ranged from 85 minutes to 249 minutes (Mussatto et al., 2014; Beca et al., 2013; Brosig Soto et al., 2011; Acton et al., 2011; Hoskoppel et al., 2010; Knirsch et al., 2010; Matsuzaki et al., 2010; Joynt et al., 2009). It was evident in reviewing these studies that the duration of CBP was longer in studies including participants with more severe CHD undergoing complex cardiac surgeries. Both the median and average duration of CPB in this study fell within the ranges reported in the literature.

The median aorta cross-clamp time in this study was 76 minutes and the average cross-clamp time was 70.3 minutes. Cross-clamp time was reported less frequently in the literature. Median cross-clamp times reported range from 40 minutes to 81 minutes (Schaefer et al., 2013; Long et al., 2012a; Long et al., 2012b; Von Rhein et al., 2012; Joynt et al., 2009). Whilst average cross-clamp times reported range from 53.6 minutes to 82.3 minutes (Acton et al., 2011; Joynt et al., 2009; Knirsch et al., 2010). The mean and median aorta cross-clamp times in this study fell within the ranges reported in the literature.

The majority of the participants in this study had a cardiothoracic ICU length of stay of one week or less. The median cardiothoracic ICU length of stay was six days, and the average length of stay was 7.5 days. ICU length of stay ranged between three and 28 days. The ICU length of stay in this study is comparable to the ICU length of stay reported in the literature, which ranged from two to seven days (Beca et al., 2013; Long et al., 2012a; Von Rhein et

al., 2012; Matsuzaki et al., 2010; Simons et al., 2010).

Post-operative hospital length of stay in this study exceeded two weeks in 21.1% of children. The median hospital length of stay post-surgery was nine days, with the average hospital length of stay 14.7 days. Making direct comparisons with hospital length of stay reported in the literature was complicated by the fact that the criteria for calculating hospital length of stay varied considerably between studies. Total hospital length of stay from admission was also not considered an accurate reflection of a complicated medical course in the current study setting, as many of these children may have had an extended period of hospitalisation prior to cardiac intervention due to social rather than medical reasons.

Reported median hospital length of stay in the literature ranged between 16 and 43 days (Mussatto et al., 2015; Mussatto et al., 2014; Schaefer et al., 2013; Long et al., 2012a; Brosig Soto et al., 2011; Joynt et al., 2009); whilst the average reported length of hospital stay reported ranged between 18 and 67 days (Mussatto et al., 2014; Acton et al., 2011; Brosig Soto et al., 2011; Knirsch et al., 2010; Matsuzaki et al., 2010; Joynt et al., 2009). It is evident that both the median and mean hospital length of stay in the current study was shorter than the duration of hospital stay reported in the literature. Possible reasons for the difference in duration of hospital stay may be attributed to the fact that the other studies included more children with severe CHD, which may have required a longer period of hospitalisation both before and after surgery due to a complicated medical course. Children represented in studies in developed countries may also have been admitted to hospital a few days earlier for surgery and kept in hospital slightly longer before being discharged. The overburdened healthcare system in SA makes bed capacity a limited resource. Consequently, children are discharged from hospital as soon as their medical condition allows (Alper et al., 2016).

In this study, cardiopulmonary resuscitation was required in 7.5% of children after surgery. This is comparable to the reported need for cardiopulmonary resuscitation reported in the literature, which ranged from 7 to 8.5% (Beca et al., 2013; Von Rhein et al., 2012). Other post-operative complications reported in the current study included respiratory infections, wound sepsis and hypoxic brain injury. Majnemer et al. (2009) also reported similar post-operative complications.

From the aforementioned discussion, it can be concluded that the CHD profile and surgical outcomes of the children in the current study are similar to those reported in the literature for children in developed countries.

6.5 Growth outcomes

6.5.1 Growth outcomes as reflected by z-scores

Growth failure and feeding difficulties are common in children with CHD, especially prior to cardiac intervention (Medoff-Cooper et al., 2016). This was affirmed by the findings in the current study where the majority of children (68%) had suboptimal growth (z-score < -2) at one or more of the time-points of assessment.

In addition, caregivers reported feeding difficulties in a quarter of participants. Feeding difficulties in this study could be attributable to CCF, DS and GORD. Similar reasons for feeding difficulties in children with CHD were put forward by Medoff-Cooper et al. (2016). Formal feeding assessment was not a study objective, and it is very likely that the prevalence of feeding difficulties was underreported in the current study. None of the children in the current study received supplemental tube feeding prior to cardiac intervention, nor were any children discharged home on tube feeds.

Growth was suboptimal in the majority of children in the current study prior to cardiac intervention, with 68% presenting with malnutrition. Of the children presenting with malnutrition, 43.5% had severe malnutrition. Stunting also occurred in 45% of the children. Growth outcomes improved post-cardiac intervention and over the study period. However, at six months post-cardiac intervention 40.9% of the children still had malnutrition, and 36.4% were still stunted.

The prevalence of malnutrition and stunting in children with CHD in developing countries has been reported to be high. Okoromah et al. (2011), in a study done in Nigeria, reported the prevalence of malnutrition as 90.4% in their study, with 61.2% having severe malnutrition. Stunting occurred in 20.5% of participants. Lata et al. (2015), in a study done India, reported that 57.3% of their study participants presented with significant growth failure

prior cardiac intervention. Vaidyanathan et al. (2008) similarly reported significant growth failure in children awaiting cardiac intervention in India. Varan et al. (1999), in their study in Turkey, also found malnutrition to be prevalent, with 65.2% of children in their study being malnourished and 52% stunted. Reported growth failure in children with CHD in developed countries ranges between 20 and 50% (Medoff-Cooper et al., 2016; Costello et al., 2015; Irving, 2011).

Rates of growth failure in children in the current study were higher than those reported for developed countries, but comparable to the growth outcomes published for children with CHD living in developing countries. Reasons for growth failure in the current study are similar to those reported in other studies done in developing countries, and are related to both SES and level of maternal education. Walker et al. (2007) suggested that poverty was associated with growth failure in children in developing countries, estimating that a third of children younger than five years in developing countries had growth retardation or stunting. In support of the aforementioned conclusion Amakali and Small (2013) similarly found that in Namibia the low SES of families of children with CHD, and low levels of maternal education, resulted in a lack of knowledge regarding a suitable cardiac diet. Insufficient financial resources also resulted in caregivers being unable to purchase adequate foods of high nutritional value. Undiagnosed and untreated feeding dysfunction may also have contributed to growth failure in the current study (Medoff-Cooper et al., 2016).

Vaidyanathan et al. (2008) also suggested that growth failure prior to cardiac intervention in children with CHD could also be attributed to haemodynamic factors related to the CHD, the presence of CCF, recurrent respiratory infections, reduced potential for growth (low birth weight) and older age at corrective surgery. Similar contributing factors were identified in the current study prior to cardiac intervention. Participants in the current study were not operated on in the neonatal period, 55% of the participants presented with CCF, 62.5% of the participants were hospitalised with respiratory-related illnesses prior to cardiac intervention and 25% had low birth weights.

Daymont et al. (2013) reported decreased growth trajectories for weight, height, as well as head circumference, identifying that children with CHD were more likely to present with microcephaly. Twenty-five percent of the participants in the current study had z-scores for

head circumference-for-age of lower than -2 prior to cardiac intervention. Possible reasons for the poor head circumference growth in the children in the current study could include malnutrition, genetic comorbidity and the cardiac disease itself. Reports on the prevalence of microcephaly in children with CHD before cardiac intervention vary in the literature, and ranges from 8 to 36% (Marino et al., 2012; Brosig Soto et al., 2011; Goldberg et al., 2011; Long et al., 2011; Hoskoppel et al., 2010; Majnemer et al., 2009). The occurrence of microcephaly in the current study was within the range reported in the literature. The prevalence of microcephaly declined over the study period, and by the six-month post-cardiac intervention 13.6% of the children still presented with microcephaly. Majnemer et al. (2009) similarly reported that microcephaly continued to persist in some children after cardiac intervention.

6.5.2 Change in growth outcomes over time

In the current study, growth outcomes improved post-cardiac intervention and over time. There was a significant positive change in weight ($p= 0.04$) and head circumference ($p= 0.02$) from baseline to the six-month post-cardiac intervention. By the six-month post-cardiac intervention, median and mean z-scores for all growth parameters fell within the acceptable range. However, complete catch-up growth had not yet occurred by the six-month post-cardiac intervention, as mean and median z-scores for all growth parameters still fell below the 50th percentile. In addition, 31.8% of the children still presented with severe malnutrition at the six-month post-cardiac intervention.

Daymont et al. (2013), Knirsch et al. (2010) and Vaidyanathan et al. (2008) similarly reported that significant catch-up growth took place after cardiac surgery. Daymont et al. (2013) also established that despite significant catch-up growth, complete catch-up growth had not yet taken place by 36 months of age in children requiring cardiac intervention, indicating a sustained decrease in the growth trajectories in children with CHD when compared to their healthy same-aged peers.

Several authors reported growth failure in children with CHD post-cardiac intervention, as was the case in the current study. Brosig Soto et al. (2011) reported growth failure to be considerably more than expected post-cardiac surgery, reporting malnutrition in 22.1% and

stunting in 15.9% of their study participants. Medoff-Copper et al. (2016) noted that 30% of their participants presented with growth failure at three-month post-cardiac intervention. Mussatto et al. (2014) reported that 54% of their study participants presented with growth failure at any of their visits. Vaidyanathan et al. (2008) noted that despite improvement in growth post-cardiac intervention 59% of the children in their study were found to be malnourished and 24.2% stunted. Malnutrition and stunting were found to be severe in 27.7% and 24.2% of cases respectively.

6.5.3 Relationship between growth and neurodevelopmental outcomes

Growth (weight) prior to cardiac intervention was significantly associated with motor developmental outcome before cardiac intervention (p= 0.04) in the current study. However, growth was not found to be strongly associated with neurodevelopmental outcome after cardiac surgery at either three-month or six-month post-cardiac intervention. Growth failure has been identified as a risk factor for poor developmental outcome (Lata et al., 2015; Irving, 2011). The strong association between growth failure and motor developmental outcomes before cardiac intervention in the current study could be explained by the fact that malnutrition was most profound prior to cardiac intervention and was likely to have resulted in muscle weakness and a lack of energy required by these children for typical age–related developmental activities. Children were likely to tire easily and this may have negatively affected the achievement of age-appropriate motor milestones before cardiac surgery. Long et al. (2011) cited similar reasons for the lack of achievement of gross motor milestones in their study on the motor developmental outcomes of children with CHD.

Knirsch et al. (2010) found that the pre-operative weight was not associated with neurodevelopmental outcome post-cardiac intervention at one year of age, which is in line with the findings in the current study. Medoff-Cooper et al. (2016) contradicted these findings, reporting a significant association between growth after cardiac intervention before the age of 30 days and neurodevelopmental outcomes at both six months and twelve months of age post-cardiac intervention. The difference in findings could possibly be attributed to the fact that the study sample of Medoff-Cooper et al. (2016) contained considerably more children with single ventricle physiologies. This is consistent with the report by Ravishankar et al. (2013) from the Paediatric Heart Network Infant Single Ventricle

Trial where growth in the first year of life was associated with neurodevelopmental outcomes at 12 months of age.

6.6 Neurodevelopmental outcomes

Developmental outcomes in the current study will only be directly compared to studies that made use of the BSID-III as their measure of neurodevelopmental outcome. It is acknowledged that there are only a limited number of neurodevelopmental outcome studies that can be used for direct comparison. Where indicated broader comparisons will be made to neurodevelopmental outcomes established by other measures.

6.6.1 Developmental performance on the BSID-III

The median age of participants at baseline was 7.4 months (mean age of 9.2 ± 5.4 months) and by the six-month post-cardiac intervention assessment 15 months (mean 16.7± 6.4 months). The age of participants and the time points of neurodevelopmental assessment in other comparable neurodevelopmental outcome studies varied considerably. The average age of children at assessment ranged from 7.2 to 27.6 months (Alsaied et al., 2016; Mussatto et al., 2015; Mussatto et al., 2014; Beca et al., 2013; Long et al., 2012a; Acton et al., 2011; Brosig Soto et al., 2011; Visootsak et al., 2011).

Mean composite cognitive, language and motor scores in the current study were below one SD (score <85) from the test mean subscale score of 100 across all three subscales of the BSID-III, at all three of the time points of assessment, apart from the language subscale at baseline and three-month post-cardiac intervention. Mean composite scores in this study across the three time points of assessment ranged between 83.4 and 84.9 (with scores ranging between 55 and 130) for the cognitive subscale, 83.4 and 90.5 (with scores ranging between 50 and 115) for the language subscale, and 79.5 and 84.3 (with scores ranging between 46 and 121) for the motor subscale. It is evident from the wide range of composite scores on all three subscales that there was considerable variation in the developmental performance of the children in the current study. Similarly Mussatto et al. (2015) and Acton et al. (2011) reported a wide variation in developmental performance of children with CHD despite them having similar clinical backgrounds. It must also be acknowledged that there

is considerable variability in skill acquisition in typically developing children, perhaps further suggesting that this variation in developmental outcome may be magnified in children with CHD (Snookes et al., 2010).

Comparing mean composite scores in the current study with those reported in the literature, Brosig Soto and colleagues (2011) in their study in the US reported mean composite cognitive scores of 100.8 ±11.9, language scores of 96 ±12.7, and motor scores of 88.6 ±18.6. They included participants with genetic comorbidity, and developmental assessment took place in infancy. Children in their study scored higher mean composite scores across all developmental domains compared to the children in the current study.

Acton and colleagues (2011) in their study in Canada, reported mean composite cognitive scores of 95.9 ±14.1, language scores of 90.8 ±18.1 and motor scores of 93.7 ±14.2. Their study excluded children with genetic comorbidity. Children in their study also scored higher mean composite scores across all developmental domains compared to the children in the current study.

Beca and colleagues (2013), in their study in New Zealand, reported mean composite cognitive scores of 94 ±15, language 94 ±16, and motor 97 ±12 Their study excluded children with genetic comorbidity. Participants were nearing two years of age in their study at the time of their assessment. Similar to the finding in the current study, language scores were lowest in their study at the six-month post-cardiac intervention where children were older. Children in their study also scored higher mean composite scores across all developmental domains compared to the children in the current study.

Long and colleagues (2012a), in their study in Australia, failed to report specific mean composite score values, but reported median composite cognitive score of 105 (with a range of 65 to 105), and language score of 106 (with a range of 65 to135). Motor composite scores were not reported. However, it was noted that the median composite scores for all three of the subscales of the BSID-III were within one SD of the test mean, which is similar to the findings noted in the aforementioned studies. More than 80% of their study participants scored within the normal limits on each of the three subscales of the BSID-III. Their study excluded children with genetic comorbidity. Participants were nearing two years of age in

their study at the time of assessment. Median scores here were higher than the mean scores reported in any of the other studies. Children in their study scored higher mean composite scores across all developmental domains compared to the children in the current study.

The current study and studies by Mussatto et al. (2015) and Mussatto et al. (2014) were the only studies where multiple assessments were performed with at least three assessments on the BSID-III. The studies by Mussatto et al. (2015) and Mussatto et al. (2014) however only reported categories of outcome, and no specific mean composite scores for these samples were reported. They did however indicate that the children in their study with CHD had stable developmental trajectories with performance in the low average range. This would also mean that children in the current study's developmental performance was poorer across all developmental domains.

It is important to highlight that children in the current study consistently attained lower scores for cognition, language and motor performance than reported in any of the other studies on the BSID-III However, mean composite scores reported in most of the other studies need to be interpreted with caution as most of these studies excluded participants with genetic comorbidity. Mussatto et al. (2015), Mussatto et al. (2014) and Brosig Soto et al. (2011) included children with CHD with genetic comorbidity and reported them to score significantly lower across all subscales of the BSID-III when compared to children with CHD without genetic comorbidity. It would therefore stand to reason that including children with genetic comorbidity in one's sample would most likely lower the mean composite scores across all developmental domains. It therefore makes only the mean composite scores reported in the study by Brosig Soto and colleagues (2011) truly suitable for direct comparison. Even if the BSID-III scores of the current study are exclusively compared to those reported by Brosig Soto et al. (2011), mean composite scores across all of the three subscales of the BSID-III in the current study are still lower. A valid conclusion can therefore be drawn that the developmental performance of children with CHD in SA is poorer than that of children in developed countries.

Poorer developmental performance across all domains of development would suggest that other factors, apart from the cardiac disease itself and the treatment thereof, contributed to the developmental outcome of the children in this sample. As no comparative BSID-III

outcome data is available for children with CHD in developing countries, the difference in outcomes are most likely attributable to factors widely reported in the literature to have a detrimental effect on childhood development in developing countries.

It is therefore plausible to consider that low SES and poverty, malnutrition, low levels of maternal education and increased levels of parenting stress contributed to the extent of the developmental delays in the children in the current study. This aligns with the multiple risks identified by Grantham-McGregor et al. (2007) and Walker et al. (2007) in *The Lancet* (2007) series on childhood development in developing countries. This view is strengthened by a recent publication by Sena Leal and colleagues (2016) who found that low levels of maternal education and low SES negatively impact the motor development in children with CHD in Brazil.

Intrinsic and individual characteristics' of the child such as genetic make-up, motivation personality and gender, could also have had an impact on the development of the children in the current study (Aubert, 2015; Rademeyer and Jacklin, 2013). Although none of the children in this study were known to be HIV-positive the HIV-status of nearly a third of the children was unknown. It is possible that there were children with undiagnosed HIV co-infection in the current sample. It would therefore be important to note that HIV infection could have contributed to the extent of the developmental delays in this sample. HIV-infection in infancy can lead to encephalopathy and an increased risk of developmental delays (Rademeyer and Jackline, 2013; Potterton et al., 2010; Baillieu and Potterton, 2008; Walker et al., 2007).

6.6.2 Prevalence of developmental delays

In the current study, 59% of the children scored below one standard deviation of the mean (score < 85) on at least one of the BSID-III subscales across the study period, indicating that they were either at risk of, or presented with developmental delays. Prior to cardiac intervention, 35% of the children in the current study presented with a developmental delay (score <70) in at least one area of development, and by the six-month post-cardiac intervention this had declined to 27.3%. There were however several participants who

presented with delays in more than one area of development both before and after cardiac intervention.

The number of children at risk and those presenting with developmental delays in the current study sample was high when compared to the prevalence of developmental delays in healthy children, which is estimated at around 16% (Mussatto et al., 2014). Reports on the prevalence of developmental delays in children with CHD vary considerably. The variable prevalence could in part be accounted for by the varying criteria used to classify developmental delay, as well as the heterogeneity of the study samples and different methodologies used in the research studies. The current study made use of the criteria set out in the BSID-III manual where scores of 70-84 were considered to be “at risk” and scores less than 70 were considered as “delayed”. Mussatto et al. (2015) and Mussatto et al. (2014) reported using a similar classification system for identifying children in need of EI referral.

Mussatto et al. (2014) reported a high prevalence in their study cohort of children being either at risk of, or presenting with delayed development, finding 75% of their participants had scored less than one standard deviation from the test mean; whilst Mussatto et al. (2015) reported delayed development in at least one domain in 34% of their study participants. Brosig Soto et al. (2011) reported that 44% of their participants scored below one standard deviation of the test mean on at least one of the Bayley subscales. Long et al. (2012a) found that only 19.1% of their participants scored below one standard deviation of the test mean in at least one area of development. The prevalence of children at risk of and those with developmental delays in the current study fell within the range reported in the literature, and was similar to that reported by Mussatto et al. (2015) and Mussatto et al. (2014) using the same classification system.

In the current study, developmental delays were mild to moderate in nature in most cases; however, severe delays were noted in some children, most especially in those with DS. The nature of the developmental delays were similar to reports by Mussatto et al. (2015) and Long et al. (2012a).

6.6.3 Developmental profile

The area of weakest developmental performance was motor development, followed by cognitive development. Language development was found to be within the norm for age prior to cardiac intervention. The current study's findings regarding the nature of the developmental delays were consistent with those reported in the literature (Long et al., 2015; Mussatto et al., 2014; Tabbutt, 2013; Sananes et al., 2012; Long et al., 2012a; Long et al., 2012b; Snookes et al., 2010).

Poor motor performance prior to cardiac intervention in the current study could be attributed to muscle weakness due to malnutrition, hypotonia, cardiovascular compromise, immobilisation, maternal overprotection and DS. Long et al. (2011) noted similar risk factors for gross motor dysfunction in their study. As also suggested by Long et al. (2012b), cardiovascular compromise likely limited the physical endurance of the children in the current study compromising their gross motor skill acquisition.

Motor development was found to improve over time and after cardiac intervention in the current sample of children. This was also consistent with the findings of Mussatto et al. (2014) and Hoskoppel et al. (2010). Possible reasons for the improvement in motor performance post-cardiac intervention could include improved strength due to increased activity and growth catch-up, resolution of the hypotonia, improved cardiovascular endurance, and less maternal over-protection.

Cognitive function was relatively unimpaired in the younger children in the current study, which was similar to the finding of Hoskoppel et al. (2010). The profile of the developmental problems in the current sample changed over time. Cognitive, but especially language, performance of children in this sample declined over time and with increasing age. This compared to the findings of Mussatto et al. (2014), Long et al. (2012a), Acton et al. (2011), and Brosig Soto et al. (2011). Increasing language skill complexity with age could provide an explanation for this finding in current as well as in the other studies.

Long et al. (2015) and Mussatto et al. (2014) raised a valid concern over the predictive value of early developmental findings of later developmental outcomes based on the changing

developmental expectations. Based on the findings in the current study one would have to agree as the developmental profile of the children in this study clearly changed over time and with increasing age.

Similar patterns of developmental delay were reported in studies using the BSID-II. Medoff-Cooper et al. (2016), Gaynor et al. (2015), Sananes et al (2012), Hoskoppel et al. (2010), Matsuzaki et al. (2010) and Snookes et al. (2010) all noted that motor delays were more prevalent than cognitive and language delays in young children with CHD. In most instances, the delays noted were mild in severity. Long et al. (2012b) found that up to 62% of children with CHD had atypical gross motor development in the first year of life. Sananes et al. (2012) similarly noted an improvement in motor performance over time.

Outcomes established by measures other than the BSID also reported that motor delay was greater than cognitive delay in young children with CHD (Lata et al., 2015; Chock et al. 2012; Majnemer et al., 2009).

It can therefore be concluded that the developmental profile of the children in the current study was similar to that of children with CHD in developed countries.

6.6.4 Gross motor developmental performance in prone

The median age of 7.4 months of the children in the current study at the time of their first cardiac surgery resulted in prone development being of particular interest as typically developing children would start to crawl between the ages of seven and nine months (Bayley, 2006a). Twenty-three participants (57.5%) exhibited delayed prone development, especially concerning crawling. Of the participants with delayed prone development, a median sternotomy was used as the surgical access route in 78.3% of these children. Development in prone was delayed in all of the children with DS in this study.

Only Long et al. (2012b) have specifically investigated gross motor development outcomes in young children with CHD who have undergone cardiac surgery in infancy. They reported atypical gross motor development in 62% of the children in their study during the first year

of life. Unfortunately, no descriptive information was provided on the attainment of specific milestones or functioning in the various developmental positions.

A possible explanation for delayed prone development could be that parents may have failed to place their children in prone due to respiratory compromise and fear. Post-cardiac surgery sternal precautions are limiting and often parents are uninformed of when they can start placing their child in prone again following cardiac surgery. Even when safe to do so, discomfort and irritability of the child when placed in prone may have prevented parents from placing their child in this position. Long et al. (2011) agreed, having found that pain sensitivity and discomfort over the sternum after open-heart surgery resulted in the failure to position infants with CHD in prone, resulting in delayed acquisition of motor milestones.

Motor development may also have been influenced by cultural practices (Rademeyer and Jacklin, 2013; Angulo-Barroso et al., 2011) African cultural practices such as carrying a baby on the mother's body may have influenced the time these children spent in prone. According to Russel et al. (2009) nearly three-quarters of the African babies in their study spent less than 10 minutes awake time in prone each day. Although cultural differences are well accepted for gross motor development, it is suggested gross motor milestones requiring more coordination and greater motor control, such as crawling, are least affected by cultural practiceces (WHO Multicentre Growth Reference Study Group, 2006). Despite cultural practices precocity of motor development has been reported in African cultures (Angulo-Barroso et al., 2011). Rademeyer and Jacklin (2013) found that typically developing black African urban infants in Gauteng, South Africa, performed better than their American peers on the BSID-III. Their findings support previous claims of African infant developmental precocity.

Despite the lack of information on specific gross motor milestone outcomes, prone is considered an extremely important developmental position. The value of "tummy time" and achieving developmental milestones in prone in children with CHD was affirmed by Long et al. (2015), who used age-inappropriate prone development as a criteria for referral to EI physiotherapy services.

6.6.5 Significant neurological sequelae

In the current study, one participant suffered a thrombotic stroke post-cardiac surgery resulting in a dense left hemiplegia. This significantly impaired developmental performance across all areas post-cardiac intervention. Long et al. (2015) and Beca et al. (2013) reported similar findings.

6.6.6 Qualification for access to early intervention services based on developmental performance

BSID-III scores can be used to identify children who would qualify for EI services. This criterion for determining eligibility for EI services is applied in clinical practice in developed countries, and is recommended in the AHA guidelines on the management of development in children with CHD (Mussatto et al., 2014; Marino et al., 2012; Brosig Soto et al., 2011). Children who score below one SD of the test mean on any of the BSID-III subscales (cognitive, language and motor) would qualify for referral to the appropriate EI services. This would therefore include children at risk of- and those presenting with developmental delays (Mussatto et al., 2014; Brosig Soto et al., 2011).

It was determined that 59% of the participants in the current study would qualify for EI services based on the set criteria; with 42.5% requiring OT, 59% ST, and 55% PT services. In many instances, children would need to access multiple therapy services to address concerns in more than one area of development.

Parents in the current study were asked to report on the referral to, and accessing of EI services. Several children were referred to EI services based on their developmental performance. It was determined that 37.5% had been referred to, or were accessing EI services to address identified developmental delays. Twenty percent had been referred to PT, 25% to OT, and 7.5% to ST services.

The identified need for and access to EI services for children with CHD varied in the literature. Brosig Soto et al. (2011) reported that 51.6% of children in their study were accessing EI services. Hoskoppel et al. (2010) reported a referral rate of 54% to EI services.

Kendall et al. (2003) and Lewin et al. (2002) noted that the rehabilitation needs were being discussed in only 41% of children with CHD in the UK. Mussatto et al. (2014) noted that 74% of children in their study had or were receiving EI services.

In the current study, 80% of the children with CHD with DS were accessing EI services, which in most cases was only OT. Brosig Soto et al. (2011) reported that in their study 100% of children with CHD with genetic comorbidity were accessing EI services. A possible explanation for the disparity in the accessing of EI services between children with CHD without and with genetic comorbidity (such as DS) could be explained by the fact that the developmental needs of children with DS, as was also shown in the current study, are greater. The specific developmental needs of children with DS are perhaps also better known to healthcare professionals, and referral systems and services for children with DS are better established within the healthcare sector than those for children with CHD without DS.

Applying the same criteria for the accessing of EI services as applied in developed countries assisted in quantifying the need for EI services in the current study population in central SA. Even developed countries with considerable healthcare resources such as the US have reported that EI programmes are extremely costly to run and that current staffing levels cannot meet the service needs (Johnson et al., 2014; Rosenberg et al., 2013; Brosig Soto et al., 2011).

Children with CHD and their families in SA are likely to face several barriers in accessing EI services. In developing countries there is insufficient health funding to provide adequate services (WHO, 2015). Furthermore, human resources for the provision of rehabilitation services are often a neglected component of healthcare services in developing countries, despite the considerable need based on the burden of disease (Gupta at al., 2011). There is also a significant disparity in access to rehabilitation services between the public and private healthcare sector in SA (Mars, 2011).

Mars (2011) reported in the South African public health sector there are 2.5 physiotherapists and two occupational therapists per 100 000 people. Similarly, speech therapists are also in short supply (Republic of South Africa, 2014). There is a significant disparity in access to

rehabilitation services between the public and private healthcare sector in SA. In the private health sector, there are 53 physiotherapists and 30 occupational therapists per 100 000 people served respectively; this being similar to ratios reported in developed countries (Mars, 2011).

6.6.7 Change in developmental outcomes over time

There were no significant changes noted in neurodevelopmental outcomes before and after cardiac intervention and over time (by three-month and six-month post-cardiac intervention) in the current study. Motor performance tended to improve over time and post-cardiac intervention, whereas cognitive and language performance tended to decline. Reasons for the lack of significant changes seen in developmental outcome over the study duration could be attributed to the relatively short time frame of the follow-up of only six-months and the relatively small sample size. A further reason could be that the developmental trajectory of most of the participants continued to be average or slightly below average over the duration of the study. This is in line with the reported average developmental trajectories over time by Mussatto et al. (2015).

6.6.8 Variables associated with neurodevelopmental outcomes

Disease severity was found to be significantly ($p= 0.02$) associated with cognitive development prior to cardiac intervention. This is similar to the findings in the literature as reported by Gaynor et al. (2015), Mussatto et al. (2015), Marino (2013), Martinez-Biarge et al. (2013), Long et al. (2012b), Sananes et al. (2012), Tabbutt et al. (2012), Goldberg et al. (2011), Long et al. (2011), Hoskoppel et al. (2010) and Simons et al. (2010). They all indicated the more severe forms of the disease were associated with poorer cognitive development.

Age at first surgery was found to be significantly associated with language development prior to cardiac intervention ($p< 0.001$) and at three-month post-cardiac intervention ($p=0.04$). The majority of children in this study underwent their first cardiac surgery in infancy at a median age of 7.5 months. These findings are in agreement with the literature, indicating that cardiac surgery in infancy is associated with poorer developmental outcomes (Gaynor

et al., 2015; Marino, 2013; Marino et al., 2012; Long et al., 2011; Donofrio and Massaro, 2010; Snookes et al., 2010; Majnemer et al., 2009; Dittrich et al., 2003). To the contrary Mussatto et al. (2014) did not report age at first open-heart surgery to be significantly associated with developmental outcome. No clear reason could be established to explain the difference in their reported finding.

In the current study, a diagnosis of DS in addition to CHD was found to be significantly ($p<0.001$) associated with poorer developmental outcome across all developmental domains, both before and after cardiac intervention. These findings are consistent with reports in the literature that indicate that the presence of a genetic abnormality is a significant and independent risk factor for adverse neurodevelopmental outcome in children with CHD (Alsaied et al., 2016; Medoff-Cooper et al., 2016; Gaynor et al., 2015; Mussatto et al., 2015; Naguib et al., 2015; Mussatto et al., 2014; Martinez-Biarge et al., 2013; Marino et al., 2012; Tabbutt et al., 2012; Brosig Soto et al., 2011; Goldberg et al., 2011; Long et al., 2011; Visootsak et al., 2011; Fuller et al., 2009; Joynt et al., 2009).

Growth (weight) was found to be significantly associated ($p= 0.04$) with motor development prior to cardiac intervention. The association between growth retardation and gross motor development can be explained by the same reasons put forward by Long et al. (2011) in that children presenting with malnutrition are also likely to be too tired and too weak, and have too little energy to engage in typical age-appropriate developmental activities, which then results in the delayed acquisition of motor skills. Similarly, Medoff-Cooper et al. (2016), Mussatto et al. (2015), Lata et al. (2015), Ravishankar et al. (2013), Brosig et al. (2014) and Long et al. (2011) all reported growth failure to be associated with poorer developmental outcomes, especially prior to cardiac intervention. Similar to Knirsch et al. (2010) and Mussatto et al. (2015), the current study found that growth (weight) was not significantly associated with developmental outcome after cardiac intervention and over time. This could be explained by the significant catch-up growth that occurred post-cardiac intervention in the children in the current study.

In the current study, maternal age was found to significantly associated with cognitive development ($p=0.01$) and motor development ($p<0.001$) before and after cardiac surgery, and over time. Maternal age has not previously been reported in the literature as a risk factor

for poorer neurodevelopmental outcome. The association between older maternal age and poorer developmental outcome in the current study could be explained by the fact that children with the poorest developmental outcome were those with DS. The mothers of the children with CHD with DS in the current study tended to be older than the mothers of the children with CHD without DS. In addition, the association may not have previously been made, because the majority of the outcome-based studies excluded children with genetic abnormalities.

The level of maternal education, which may also serve as a proxy for SES, showed a near significant (p=0.05) association with cognitive development after cardiac intervention in the current study. This would be consistent with the findings by Gaynor et al. (2015), Mussatto et al. (2015), Tabbutt et al. (2012) and Majnemer et al. (2009) who found lower levels of maternal education to be associated with poorer cognitive development. Low levels of maternal education and poor SES could negatively affect cognitive development through the lack of suitable stimulation in the home environment and lack of responsive parenting (Engle et al., 2007; Walker et al., 2007). To the contrary, Mussatto et al. (2014) found the level of maternal education and SES not to be a strong predictor of developmental outcome. The finding of Mussato et al. (2014) could possibly be explained by the fact that the majority of their study participants came from a middle-class or affluent communities, and parents were generally well educated. The lack of variability in SES in their study might not have reflected the impact of low SES and low levels of maternal education on developmental outcome.

In the current study, SES itself was not found to be significantly associated with developmental outcome. These findings are contrary to the findings of Gaynor et al. (2015), Mussatto et al. (2015), Naguib et al. (2015), Sarrechia et al. (2015), Sananes et al. (2012), Tabbutt et al. (2012), Von Rhein et al. (2011) and Majnemer et al. (2009) who all found lower SES to be associated with worse developmental outcomes. The lack of association shown between SES and developmental outcome in the current study could perhaps be attributed to the fact that almost all families were from the same socioeconomic class (low class). Thus the true impact of varying SES could not be captured in the current study sample.

Increased cardiac ICU length of stay, increased duration of mechanical ventilation, and increased hospital length of stay served as proxy for a complicated medical disease course. None of the aforementioned factors were found to be significantly associated with developmental outcome in the current study. This is contradicted by the findings of Medoff-Cooper et al. (2016), Mussatto et al. (2015), Ravishankar et al. (2013), Long et al. (2012b), Marino et al. (2012), Sananes et al. (2012), Von Rhein et al. (2012) and Long et al. (2011) which indicated that a prolonged hospital length of stay and a complicated medical course were associated with worse developmental outcomes. It is important to note that these studies included a high proportion of children with cyanotic heart defects, and many included complex lesions involving single ventricle physiologies. The contradictory findings may therefore be explained by the fact that the majority of the children in the current study had acyanotic lesions and disease severity in most cases was moderate. It is therefore reasonable to conclude that the children in the current study were less likely to have followed a complicated medical course requiring prolonged ICU and hospital length of stay.

Duration of CPB was also not found to be significantly associated with developmental outcome in the current study. This is contradicted by the findings of Mussatto et al. (2015), Mussatto et al. (2014), Marino et al. (2012), Sananes et al. (2012), Tabbutt et al. (2012), Bellinger et al. (2011), Hoskoppel et al. (2010) and Simons et al. (2010) which indicated that a longer duration of CBP was associated with worse developmental outcome. A possible explanation for the contrasting findings could be that the aforementioned studies included a large number of children with severe disease who were likely to require complex cardiac surgeries and longer durations on CPB than the children in the current study.

The current study did not find gestational age at birth or birth weight to be significantly associated with developmental outcome. To the contrary, Chock et al. (2012), Sananes et al. (2012) and Goff et al. (2011) all noted prematurity and low birth weight to be associated with worse developmental outcomes. Both Gaynor et al. (2015) and Mussatto et al. (2014) similarly found that gestational age was not strongly associated with neurodevelopmental outcome. A possible explanation for the contradictory findings could have been the varying patient profiles of the children included in the aforementioned studies. The birth weight and gestational age at birth of most the children in the current study were within the normal range, perhaps explaining the lack of association between these variables and

developmental outcome.

Gender was not found to be strongly associated with developmental outcome in the current study. Few studies have reported on the association of gender with developmental outcome; however, Gaynor et al. (2015), Sananes et al. (2012) and Majnemer et al. (2012) reported that male gender was associated with poorer developmental outcome, especially relating to cognitive and fine motor skills. The difference in findings in the current study could potentially be explained by the small sample size and the fact that there were more female than male participants.

6.7 Neurological findings

Hypotonia was the only significant abnormal neurological finding in the current study. This was consistent with reports in the literature by Lata et al. (2015), Majnemer et al. (2009) and Limperopoulos et al. (2000).

Forty-five percent of the participants in the current study presented with hypotonia at baseline and at three-month post-cardiac intervention. This was comparable with Marino et al., (2012), Tabbutt et al. (2012), Donofrio et al. (2011) and Majnemer et al. (2009) who all reported the prevalence of abnormal neurological finding to range between 36 and 52% prior to cardiac intervention. A possible explanation for the tendency of the hypotonia to resolve over time could be that the hypotonia in most cases was secondary to muscle weakness that resulted from the considerable under-nutrition of most participants prior to cardiac intervention. The resolution of hypotonia in participants in the current study coincided with considerable improvements in growth status (weight) and motor development post-cardiac intervention, would support this hypothesis.

All children in the current study with CHD with DS presented with marked hypotonia over the duration of the study (Refer to 6.10.3)

6.8 Parents' perception of health-related quality of life

Very few studies have been done to establish HRQOL in toddlers, and even fewer in infants with CHD, which somewhat limits comparisons with the published literature. Findings from the current study will not be compared to the HRQOL outcomes of older children and adolescents, as age and developmental stage influence HRQOL, thus making these findings unsuitable for comparison.

6.8.1 Parents' perception of HRQOL outcomes as reflected by the PedsQL® scores

6.8.1.1 Health-related quality of life outcomes for children younger than two years

Parents' perception of the HRQOL outcomes of children under the age of two years in the current study was found to be good at all three time points of assessment (the total mean PedsQL ™ scores ranged from 77.6 to 85.2 over the current study). The PedsQL™ total scores at all three times of assessment in the current study were within the range of the mean scores reported by Varni et al. (2011) for healthy children aged one to 12 months (82.47 ±9.95) and children aged 13 to 24 months (85.55 ±8.74) (see Appendix XVII for tables of the results for the individual scales of the PedsQL™). Mean total PedsQL™ scores in the current study were higher than those reported by Varni et al. (2011) for children with chronic illness aged one to 12 months (68.02 ± 13.92) and children aged 13 to 24 months (69.87 ±10.37). It can therefore be concluded that HRQOL outcomes of the children in the current study to be similar to that of their healthy same-aged peers.

In the current study, parents' perceived their children's HRQOL as being similar to that of their healthy same-aged peers. This could be explained by the fact that the majority of the children in the current study had moderate disease severity. This would make it unlikely that their physical, cognitive or social-emotional functioning would be significantly impaired; therefore, their HRQOL would likely be perceived by parents to be good.

Parents viewed their children's physical health as being poorer than their psychological health prior to cardiac intervention in the current study. This would align with the developmental outcomes in the current study that found motor development to be most

affected prior to cardiac intervention. After cardiac surgery, and as the children became older, parents reported their psychological functioning to be more problematic than their physical functioning. This would also align with the developmental outcomes in the current study in that deficits in cognitive and language development became more apparent over time, and with increasing age and developmental skill complexity.

Werner et al. (2014) reported better overall HRQOL in children with CHD at the age of one year compared to their healthy peers, the reason being that younger children exhibited fewer behavioural problems and parents were simply glad that their child was active despite their CHD.

6.8.1.2 Health-related quality of life outcomes for children older than two years

Fewer heart-related symptoms were reported for children in the current study (mean scores ranged from 95 to 98.8) compared to Eagleson et al.'s (2013) study (mean scores ranged from 76.14 to 85.5). Possible reasons for this could be that most of the children in the current study had moderate disease severity, and that heart symptoms were likely to have resolved or improved considerably post-cardiac intervention. The Cardiac Module was only administered post-operatively, as all children were under the age of two years when undergoing their first cardiac surgery, so no comparison could be made on the cardiac module from before to after cardiac intervention.

Children in the current study (mean score of 56.3 ±50.5) displayed greater treatment anxiety post-cardiac intervention compared to that reported by Eagleson et al. (2013) (mean score of 87.1 ±19.1) and in other studies conducted in children aged two to 18 years using the Cardiac Module (mean score ranged from 61.08 to 87.1)(Sand et al., 2013; Uzark et al., 2013; Berkes et al., 2010; Tahirović et al., 2010; Uzark et al., 2008; Mussatto and Tweddell, 2005). This could be explained by a possible post-cardiac intervention aversion to and fear of healthcare personnel due to their association with painful procedures and other negative experiences related to cardiac care and surgery.

HRQOL outcomes in the current study relating to physical appearance (mean scores ranged from 95.8. to 100) were comparable to those established by Eagleson et al. (2013)(mean

score of 87.1 ±19.1) and in other studies conducted in children aged two to 18 years using the Cardiac Module (mean scores ranged 80.37 to 87.1))(Sand et al., 2013; Uzark et al., 2013; Berkes et al., 2010; Tahirović et al., 2010; Uzark et al., 2008; Mussatto and Tweddell, 2005). Cognition outcomes in the current study (mean score ranged from 79.1 to 100) were comparable to those established by Eagleson et al. (2013) (mean score of 81.5 ±12.3) and in other studies conducted in children aged two to 18 years using the Cardiac Module (mean scores ranged from 67.06 to 81.5)(Sand et al., 2013; Uzark et al., 2013; Berkes et al., 2010; Tahirović et al., 2010; Uzark et al., 2008; Mussatto and Tweddell, 2005). Communication outcomes in the current study (mean scores ranged from 75 to 100) were comparable to those reported by Eagleson et al. (2013) (mean score of 100) and in other studies conducted in children aged two to 18 years using the Cardiac Module (mean scores ranged from 71.58 to 80.08)(Sand et al., 2013; Uzark et al., 2013; Berkes et al., 2010; Tahirović et al., 2010; Uzark et al., 2008; Mussatto and Tweddell, 2005).

The findings in the current study were aligned with the findings of all the comparable studies reviewed, in that treatment anxiety, cognitive function, and communication ability impacted most negatively on parents' perception of their child's HRQOL in children aged two years and older. The negative impact of cognitive and language deficits on HRQOL are consistent with the developmental outcome findings in the current study, where cognitive and language delays emerged over time and with the increasing age of the child and increasing skill complexity.

The overall HRQOL of two to three year olds in the current study was comparable to HRQOL of other children with CHD aged two years and older. This was determined by the comparison of the total mean score for the PedsQL™ Cardiac Module in the current study (mean score ranged from 85.3 to 97.8) with the total mean scores reported for the Cardiac Module by Uzark et al. (2008) (mean score of 86.66 ±12.19) and Sand et al. (2013) (mean score of 80.08 ±17).

Furthermore, the HRQOL of two to three year olds with CHD in the current study was found to be comparable to that of their healthy same-aged peers. This was determined through the comparison of total mean scores on the PedsQL™ Cardiac Module with the total mean score for healthy peers on the PedsQL™ Generic Core Scales which were reported by Uzark

et al. (2008) as 87.86 ±12.19 and Berkes et al. (2010) as 79 ±15.

6.8.1.3 Health-related quality of life outcomes for all children

Parents' perception of their children's HRQOL in the current study was good, and comparable with other children with CHD as well as their healthy same-aged peers. Improved scores on the PedsQL™ post-cardiac intervention are likely to reflect the improved physical and psychosocial functioning of the children in the current study after cardiac intervention. The parents' had wide-ranging perceptions of their children's HRQOL, and across the study there were some children whose physical and psychosocial functioning negatively affected their health and wellbeing.

In general, the positive HRQOL outcomes of the children in the current study are similar to those reported by numerous investigators who found the HRQOL of children with CHD to be largely unaffected and similar to that of their same-aged healthy peers (Schaefer et al., 2013; Berkes et al., 2010; Uzark et al., 2008; Hövels-Gürich et al., 2007; Birks et al., 2006; Majnemer et al., 2006b; Goldbeck and Melches, 2005). The majority of participants in the current study had moderate disease severity, and it is reasonable to anticipate that children with more severe disease may have poorer HRQOL outcomes, based on the findings in the literature. In addition, by virtue of the fact that HRQOL is a subjective measure in young children with CHD, reflecting parents' perceptions of their child's HRQOL, could also serve to explain some of the variability in outcomes.

6.8.2 Changes in parents' perception of health-related quality of life over time

There was a significant improvement ($p=0.04$) in parents' perception of their children's HRQOL in the current study at three-month post cardiac-intervention when compared to before cardiac intervention. Improved perception of their children's HRQOL post-cardiac intervention could be attributed to a decrease in cardiac symptoms, and the improved physical and psychosocial functioning shown by many of the children in the current study after cardiac intervention. It was to be anticipated that parents would experience high levels of stress shortly before their child was to undergo cardiac surgery which might have influenced their perception of their child's HRQOL at that point in time. Decreased levels of

parental stress following cardiac intervention might therefore also have favourably changed parents' perceptions of their children's HRQOL. The current study's findings are consistent with the findings of Bertoletti et al. (2015), Marino et al. (2009) and Birks et al. (2006).

In the current study, parenting stress and parents perception of their child's HRQOL were closely linked before cardiac intervention. Parents found their child's CHD to be a source of considerable stress prior to cardiac intervention and their perception of the impact of the CHD, irrespective of the disease severity, had a considerable effect on the way they perceived their child's HRQOL. This was consistent with the findings of Bertoletti et al. (2015), Dulfer et al. (2015), Knowles et al. (2014), Eagleson et al. (2013), Spijkerboer et al. (2010), Miatton et al. (2007), Majnemer et al. (2006b) and Mussatto et al. (2006).

6.8.3 Variables associated with health-related quality of life outcomes

In the current study, motor development was significantly (p=0.01) associated with parental perceptions of their child's HRQOL prior to cardiac intervention. The reason for this finding could be that parents' felt that the limitations the cardiac disease placed on their child's physical activity, as well as other environmental restrictions, might have prevented their child from being able to perform the same age-appropriate motor activities as their healthy peers. This was consistent with reports by Bertoletti et al. (2015), Nousi and Christou (2010), Miatton et al. (2007) and Birks et al. (2006) in that CHD led to physical activity limitations.

Levels of parenting stress in the current study, prior to cardiac intervention, were also significantly (p= 0.02) associated with parents' perceptions of their child's HRQOL at the same time point. This is similar to reports by Dulfer et al. (2015), Eagleson et al. (2013), Spijkerboer et al. (2010), Miatton et al. (2007) and Majnemer et al. (2006b). As discussed under 6.8.2 parents found their child's CHD to be a source of considerable stress and their perception of the impact of the CHD on their child had a considerable effect on the way they perceived their child's HRQOL. It could be speculated that additional stressors including low SES, uncertainty about the child's health outcomes, and the increased burden of care, especially prior to cardiac intervention might also have influenced parents perception of their child's HRQOL. In agreement with Nousi and Christou (2010) parents may have projected

their own personal distress onto their child, negatively influencing their perception of their child's HRQOL.

Disease severity was not shown to have a significant association with parents' perception of their child's HRQOL. This is similar to the reported findings of Amedro et al. (2015), Bertoletti et al. (2015), Latal et al. (2009) and Majnemer et al. (2006b). It is acknowledged that the impact of disease severity on parents' perception of their child's HRQOL remains controversial. Disease severity itself has proven an unreliable predictor of HRQOL outcomes in young children with CHD, and perhaps rather, as Mussatto (2006) suggests, parental perception of the impact of the CHD on their child might play a more important role in determining parents' perception of their child's HRQOL.

The current study's findings however, contradict those of Eagleson et al. (2013), Sand et al. (2013), Tahirović et al. (2010) and Uzark et al. (2008) who all found disease severity to be significantly associated with parents' perception of their child's HRQOL. Macran et al. (2006), in turn, only found disease severity to influence HRQOL outcomes in younger children. The reason for the contradictory findings most likely lies in the participant profile of the aforementioned studies with regard to disease severity and age of the children.

Similar to Hövels-Gürich et al. (2007), the current study did not find the type of CHD (presence of cyanosis) to be significantly associated with HRQOL outcomes. The current study's finding contradict the findings of Schaefer et al. (2013), Tahirović et al. (2010) and Birks et al. (2006) who found that the presence of cyanosis negatively influenced HRQOL outcomes. The contradictory findings with regards to the impact of cyanosis on HRQOL could be attributed to the varying patient profiles reflected in the aforementioned studies. A possible reason for the lack of association shown between cyanotic heart disease and HRQOL outcomes in the current study could be ascribed to the fact that the majority of the children in the current study had acyanotic heart defects.

In the current study, surgical variables including age at first cardiac surgery and duration of CPB were found not to be significantly associated with HRQOL outcomes. This study's findings regarding the association of age at first cardiac surgery with HRQOL outcomes contradicts the findings of Latal et al. (2009) who found that older age at first cardiac surgery

was associated with worse HRQOL outcomes. The contradictory findings could be explained by the fact that Latal et al. (2009) included children of a far wider age range and older age at their first cardiac surgery. Similar to the findings in the current study, Majenemer et al. (2006) found that surgical factors were not strong predictors of HRQOL outcomes in children with CHD. This study's findings are contradicted by the findings of Schaefer et al. (2013), Latal et al. (2009) and Hövels-Gürich et al. (2007) who reported a significant association between the duration of CPB and HRQOL outcomes. A possible explanation for the contradictory findings could be the varying patient profiles represented in the aforementioned studies, in particular relating to disease severity. It is possible that children with more severe disease in the other study samples may have required surgeries that were more complex, thus requiring a longer duration of CBP. These children could have had different HRQOL outcomes compared to children in the current study, where most children had moderate disease severity and less complex defects resulting in surgeries requiring shorter durations of CPB.

In the current study, patient variables including growth failure, feeding problems and the presence of DS were found not to be strongly associated with parents' perception of their child's HRQOL. This study's findings contradict those of Nousi and Christou (2010) who found growth failure in children with CHD to be significantly associated with poor HRQOL outcomes. This study's findings also contradict those of Werner et al. (2014) who reported poorer HRQOL outcomes in children with genetic abnormalities. Similarly, Garcia Guerra et al. (2014) reported significantly worse HRQOL in children with CHD with genetic abnormalities compared to both their healthy same-aged peers as well as other children with CHD without genetic abnormalities. Possible explanations for the contradictory finding in the current study regarding the association of both growth failure and genetic abnormalities with HRQOL outcomes could possibly be that parents might have viewed their child as either having a medical problem that affected their health or not. Additional problems apart from the cardiac disease, including growth, failure, poor feeding and DS might then not significantly have altered their view of their child's HRQOL.

Socioeconomic factors including SES and level of maternal education were not found to be strongly associated with parents' perception of their child's HRQOL. The findings on the association between SES and HRQOL have proven inconsistent in the literature (Uzark et

al., 2008; Mussatto, 2006). Amedro et al. (2015), Eagleson et al. (2013), Latal et al. (2009) and Nousi and Christou (2010) reported that SES was associated with the HRQOL outcomes in children with CHD. A possible reason for the contradictory findings in the current study could be that the majority of the parents had the same level of education, and were from the same socioeconomic class, thus limiting the ability to make strong associations between variable SES and educational attainment and parental perceptions of their children's HRQOL.

The association between the child's age and parents' perception of their HRQOL was not specifically investigated in the current study; however, it was evident that HRQOL improved post-cardiac intervention and over time with increasing age. This is consistent with reports by Sand et al. (2013). Eagleson et al. (2013) however found age not to be associated with HRQOL outcomes. No clear reason for the difference in findings could be identified.

6.9 Parenting stress and burden of care

Very few studies have established parenting stress in parents of infants and toddlers living with CHD. Parenting stress reported in the current study is predominantly a reflection of the parenting stress experienced by mothers. In most instances the child was accompanied by only the mother on admission and for healthcare visits; therefore the parenting stress of the fathers could not be established consistently in the current study.

6.9.1 Parenting stress outcomes

The majority of primary caregivers (60%) in the current study experienced clinically significant levels of stress in their parenting role just prior to their child undergoing cardiac surgery, This is consistent with the findings of Wei et al., (2016), Harvey et al. (2013), Landolt et al. (2011), Solberg et al. (2011) and Franck et al. (2010).

Some parents of children with chronic health conditions experience ongoing stress (Golfenshtein et al., 2016), this was also found to be the case in the current study. Even though total stress scores declined over time in the current study, just more than a third of parents experienced ongoing stress after their child's cardiac intervention. This is consistent

with the findings of Wei et al. (2016), Hearps et al. (2014), Grønning Dale et al. (2013), Harvey et al. (2013) and Goldberg et al. (1990) in that parents of children with CHD experience higher levels of stress than parents of children with other chronic health conditions, and parents of healthy children. This however contradicts the findings of Vrijmoet-Wiersma et al. (2009) that parents of children with CHD experienced similar levels of stress to parents of healthy children. Whilst, Brosig et al. (2007) provides even further contradiction by suggesting that some parents may even experience lower levels of stress compared to parents of healthy children due to the fact that they develop a higher tolerance for what is perceived to be stressful because of their experiences relating to their child's CHD.

6.9.2 Changes in parenting stress over time

Parenting stress levels in the current study declined significantly from before cardiac intervention at both three-month ($p < 0.001$) and six-month ($p < 0.001$) post-cardiac intervention. The significant decline in the levels of parenting stress can be explained by the resolution or improvement in cardiac symptoms and the improved health and wellbeing of the children after cardiac intervention. It was to be anticipated that parents would experience high levels of stress shortly before their child was to undergo cardiac intervention, this might also have contributed to the significant decrease in parenting stress post cardiac intervention. This is consistent with previous findings (Wei et al.; 2016; Grønning Dale et al., 2013). In addition, a large number of children in the current study underwent definitive corrective surgery (73.6%), leaving minimal lasting deficits (Goldberg et al., 1990). Despite the significant decrease in parenting stress over the time-span of study, it is important to note that just over a third of parents continued to experience high levels of stress after their child's cardiac intervention (Refer to discussion under 6.9.2).

6.9.3 Burden of care and parent stressors

Several stressors were identified to contribute to parenting stress and the burden of care experienced by parents in the current study. A limitation of the PSI-SF is that it only measures stressors directly related to a parent's parenting role, yet many factors outside of the parenting role may contribute to parenting stress. To negate the limitations of the PSI-

SF, parents were asked to provide information on their experience of the impact of their child's health status and medical care, socioeconomic circumstances and burden of care on the stress they experienced.

6.9.3.1 Illness-related stressors

The majority of parents found seeing their child in the cardiac ICU after cardiac surgery attached to machines and with drainage tubes to be the most stressful experience. This is consistent with the findings of Wei et al. (2016), Harvey et al. (2013), Landolt et al. (2011), Solberg et al. (2011) and Franck et al. (2010).

6.9.3.2 Parent-related stressors

Parent-related stressors included the burden of caring for a child with CHD. Mothers fulfilled the role of primary caregiver in most instances in the current study, and as a result shouldered most of the burden of care. This is consistent with the findings of Bruce et al. (2014), Grønning Dale et al. (2013), Fonseca et al. (2012), Yildiz et al. (2009), Lan et al. (2007) and Lawoko and Soares (2006). In the current study, grandmothers carried a considerable burden of care in the case of teenage mothers or where the child's mother could not fulfil the role of primary caregiver. Several mothers were unmarried and headed single-parent households. Most mothers also did not work outside of the home. This is similar to findings reported by Amakali and Small (2013) for mothers of children with CHD in Namibia. Roman et al. (2016) concurred that the burden of childcare in sub-Saharan Africa predominantly fell on mothers due to cultural practices where black African men tend not to be involved in the day-to-day care of the children.

In the current study, hospital admissions prior to cardiac intervention for respiratory complaints and employed parents having to miss work to due to their child's ill health added to the burden of care experienced by mothers in the current study.

6.9.3.3 Child-related stressors

More than half of the parents' felt that their child failed to meet their expectations. Although dysfunction in parent-child interaction improved over the time-span of the study, it remained the stressor that most contributed to parenting stress. Similar indications that parental perception of their child and acceptance of the child affect levels of parenting stress have been noted (Golfenshtein et al., 2016).

The majority of parents in the current study did not find their children demanding or difficult to parent. Parenting styles and cultural perceptions may have contributed to this view (Roman et al., 2016). In addition, the majority of children in the current study had moderate disease severity and were unlikely to be overly irritable, possibly explaining the contradictory findings of Golfenshtein et al. (2016), Soulvie et al. (2012), Torowicz et al. (2010) and Uzark and Jones (2003).

6.9.3.4 Socioeconomic-related stressors

Many of the parents in the current study highlighted the impact their current socioeconomic circumstances had on their psychosocial wellbeing. It can be speculated that unemployment, low SES, low levels of maternal education and a lack of social support exacerbated the stress parents' were already experiencing in their parenting role. This is in agreement with reports by Amakali and Small (2013), Engle et al. (2007) and Walker et al. (2007) who noted that financial strain increased levels of parenting stress in developing countries. Golfenshtein et al. (2016), Bruce et al. (2014), Harvey et al. (2013), Grønning Dale et al. (2013), Soulvie et al. (2012) and Connor et al. (2010) reported similar findings in developed countries.

6.9.4 Variables associated with levels of parenting stress

Neurodevelopmental outcome, and in particular language development, was found to be significantly associated with parenting stress prior to cardiac intervention ($p=0.04$), as well as at three-month post-cardiac intervention ($p=0.03$). One may speculate that a lack of communication and social interaction on the part of the child with a parent is likely to increase

parental anxiety and negatively affected the parent-child relationship. Similarly, several other investigators in developed countries have indicated that parenting stress negatively impacts on the quality and responsiveness of caregiving, ultimately having a detrimental effect on the child's social-emotional, motor, cognitive and language development (Soulvie et al., 2012; Landolt et al., 2011; Laing et al., 2010; Torowicz et al., 2010; McCusker et al., 2009; Fulbright Sumpter, 2009). Engle et al.'s (2007) findings in developing countries proved to be similar in this regard.

Parents' perception of their child's HRQOL was significantly ($p=0.02$) associated with levels of parenting stress before cardiac intervention. Parental perception of their child's HRQOL may be closely linked to their perception of their child's level of functioning and their view of the parent-child relationship. If parents perceive their child as having a poor ability to function in everyday situations, their stress levels are likely to increase (Mussatto, 2006).

The age of the child at first cardiac surgery ($p=0.03$) and the age of the mother ($p=0.04$) were found to be significantly associated with parenting stress at three-month post-cardiac intervention. A possible reason for this finding in this study could be the young age of the children and that the cardiac intervention was recent, which were both factors that were likely to contribute to the burden of care and therefore the level of parenting stress experienced. This is consistent with findings of Soulvie et al. (2012) and Lee et al. (2007) that parenting toddlers and pre-schoolers with CHD resulted in higher levels of parenting stress by virtue of the higher burden of caregiving in children of these ages.

Disease type and severity were not found to be significantly associated with levels of parenting stress. Parenting stress tended to be similar for the parents of the children with cyanotic and acyanotic heart defects in the current study. This is likely due to the fact that patient characteristics were similar for both groups, and the disease severity was only marginally worse in the cyanotic group. This is consistent with the reported findings of Hartman and Medoff-Cooper et al. (2012), Vrijmoet-Wiersma et al. (2009) and Mussatto et al. (2006). The current study findings contradict those of Grønning Dale et al. (2013), Torowicz et al. (2010), Connor et al. (2010), Majnemer et al. (2006b), Mörelius et al. (2002) and Goldberg et al. (1990) who reported parenting a child with severe CHD to be more stressful. The difference in findings is possibly attributable to varying participant profiles of

the aforementioned studies with regard to disease severity. Disease severity has however failed to explain parents' psychological morbidity over time (Grønning Dale, 2013). Rather, parents' perception of the impact of the CHD on their child and family may have proven to be a powerful predictor of long-term psychological morbidity in the current study, than disease severity, as has been suggested by Rempel et al. (2013).

In the current study, patient-specific factors, including DS and growth failure, were not found to be significantly associated with levels of parenting stress. This contradicts the finding of Torowicz et al. (2010) that growth failure increased the burden of care and level of parenting stress, and Visootsak et al. (2015) that the presence CHD with DS was associated with greater levels of parenting stress. The lack of association between these variables and levels of parenting stress may be a reflection on the fact that parents viewed their children as either having a medical problems or not, irrespective of the number of problems.

SES and maternal education were not found to be strongly associated with levels of parenting stress in the current study. Possible reasons for the lack of a strong association being shown may relate to the fact that the PSI-SF does not measure the impact of factors that are unrelated to the parenting role. In addition, similar SES and levels of maternal education levels across the sample, and the small sample size may also have limited the ability to show a strong associations between SES and levels of parenting stress.

6.10 Outcomes in children with Down syndrome

6.10.1 Introduction

Twenty-five percent of the children in the current study were diagnosed with DS. The representation of children with genetic abnormalities in this study are similar to that reported by Gaynor et al. (2015), Mussatto et al. (2014) and Brosig Soto et al. (2011). The median age of the mothers of children with CHD with DS in the current study was advanced at 37 years. Visootsak et al. (2011) reported a comparable maternal age. Advanced maternal age is known to be associated with an increased risk of DS (Bertoti and Schreiner, 2015; Elmagrpy et al., 2011; Murphy et al., 2006).

Due to the small sample size, no further statistical analysis was done to determine inter-group differences, as subgroups were insufficiently powered to be able to draw reasonable conclusions. However, it was deemed important to identify trends in outcomes between groups. Apart from the current study, very few studies have reported on the outcomes of children with CHD with DS. This serves to highlight the uniqueness of the current study.

6.10.2 Growth outcomes

In the current study, growth outcomes for children with CHD with DS were found to be similar to those with CHD without DS when the DS-specific growth standards were used to determine the growth outcomes of children with DS, allowing for fair comparison with their peers. The prevalence of malnutrition prior to cardiac intervention was similar for the children with CHD with and without DS. The majority of the children (60%) with CHD with DS presented with malnutrition prior to cardiac intervention, and a large number were stunted. Twenty percent of the children with CHD with DS had microcephaly. The reasons for suboptimal growth in children with CHD with and without DS in the current study are likely to be similar (Refer to 6.5.1). It is difficult to compare growth outcomes in children with CHD with DS with the published literature as available studies by Knirsch et al. (2010) and Bravo-Valenzuela et al. (2011) made use of standard growth charts to determine growth outcomes, which could mean that the extent of the growth failure reported in these studies may be overestimated.

The children with CHD with DS in the current study showed considerable catch-up growth following cardiac intervention, but complete catch up growth had not occurred by the six-month post cardiac intervention. Despite median z-scores for growth parameters falling within the acceptable range by the six-month post-cardiac intervention, the z-scores were still below the 50th percentile. This is in agreement with the findings of Bravo-Valenzuela et al. (2011). To the contrary, Knirsch et al. (2010) found the presence of a genetic abnormality to be the single most significant predictor of poor catch-up growth post-surgery. Again, possible reasons for the variable findings could be attributed to the use of standard growth charts and population means, as well as varying patient profiles with regard to disease severity.

6.10.3 Developmental outcomes

In the current study, composite scores across all three BSID-III subscales (cognitive, language and motor) at all three time-points of assessment tended to be much lower for the children with CHD with DS when compared with the children with CHD alone. This is consistent with the findings of Alsaied et al. (2016), Mussatto et al. (2014), Brosig Soto et al. (2011) and Visootsak et al. (2011).

Language and cognitive development for the children with CHD with DS in the current study declined over the course of the study, and motor development remained poor over the study duration. This is consistent with the findings of Mussatto et al. (2014). Declining cognitive and language performance over time, and with increasing age may be explained by the heightened skill complexity with increasing age and the impact of the intellectual impairment characteristic of DS (Alsaied et al., 2016; Visootsak et al., 2013; Van Gameren-Oosterom et al., 2011;Visootsak et al., 2011; Marino et al., 2012). In addition, children with DS are limited in their ability to explore their environment due to their motor impairments, which in turn may result in secondary impairments related to cognition (Bertoti and Schreiner, 2015; Visootsak et al., 2011). This study's findings are also consistent with the findings of Alsaied et al. (2016), Visootsak et al. (2013) and Visootsak et al. (2011) that children with DS present with delayed expressive and receptive language.

The extent of the motor delays in children with CHD with DS may be attributed to the marked hypotonia, joint laxity, lack of postural- and antigravity control, and deficits in both balance and coordination. These would be consistent with the reasons for poor motor performance in children with DS as suggested by Bertoti and Schreiner (2015) and Visootsak and colleagues (2011). The aforementioned causes are likely to be superimposed on other contributing factors for motor delay in children with CHD as discussed under section 6.6.3 and 6.6.4. The above-mentioned would perhaps go on to explain the greater extent and severity of the motor delays seen in the children with CHD with DS in the current study, as well as in the studies by Alsaied et al. (2016) and Visootsak et al. (2011), when compared with children with either DS alone or CHD alone.

All children with CHD with DS presented with marked hypotonia at all time points of assessment, whilst hypotonia in children with CHD without DS tended to resolve by the six-month post cardiac intervention. The marked hypotonia in children with CHD with DS is characteristic of DS (Visootsak et al., 2013).

6.10.4 Parents' perception of health-related quality of life outcomes

In the current study, when comparing the total PedsQL^{TM} scores with the normative values published by Varni et al. (2011) for healthy and chronically ill children, it is apparent that parents of children with CHD with DS perceived their children's HRQOL to be reasonably good compared to their healthy peers and marginally better than that of children with other chronic conditions. There was however a tendency of parents of children with CHD with DS to perceive their children's HRQOL as poorer than that of parents of children with CHD without DS. Parents of children with CHD with DS perceived their children's HRQOL to be largely unchanged over the time-span of the study.

Very little has been published on the HRQOL outcomes of children with CHD with DS, and there are no reported studies in children as young as the participants in the current study. Most HRQOL studies have excluded children with genetic abnormalities, as it is considered an independent risk factor for worse HRQOL. However, Garcia Guerra et al. (2014) and Werner et al. (2014) reported poorer HRQOL outcomes in slightly older children with CHD with genetic abnormalities compared to children with CHD alone. Van Gameren-Oosterom et al. (2011) found children with DS alone to have impaired HRQOL with regard to developmental functioning and autonomy.

6.10.5 Parenting stress outcomes

In the current study, half of the parents of the children with DS experienced clinically significant levels of stress just before their children underwent cardiac intervention. This was comparable to parents of children with CHD without DS, which was to be anticipated in that stress in both groups at this specific point in time was largely driven by the anxiety and fear of the impending cardiac intervention.

At both three-months and six-month post-cardiac intervention parenting stress levels tended to be considerably higher for the parents of the children with DS. This could potentially be explained by the fact that for many parents of children with CHD without DS their child's medical problem was either resolved completely or there was a significant improvement in the child's clinical picture after cardiac intervention. However, for the parents of the children with DS, despite having seen a considerable improvement in their child's cardiac symptoms, they continued to experience stress related to parenting a child with DS. This is consistent with the findings of Visootsak et al. (2015) that having a child with CHD with DS provided parents with additional stress. Parents of children with CHD with DS were found to have consistently reported higher levels of parenting stress, compared to parents of children with only DS.

6.11 Outcomes in children with cyanotic heart defects

6.11.1 Growth outcomes

Only 20% of participants in the current study were diagnosed with cyanotic heart defects. Of the children with cyanotic defects 87.5% would require further surgeries. More children with cyanotic heart defects presented with growth failure both before and after cardiac intervention compared with the children with acyanotic heart defects, and the extent of the growth retardation tended to be greater. A reason for this finding is that cyanosis results in chronic hypoxia causing dyspnoea and tachypnoea during feeding. Breathing difficulties cause the child to tire easily during feeding resulting in inadequate food and calorie intake (Roman, 2011; Da Rosa Pereira et al., 2015). Furthermore, these children are likely to be in a state of constant metabolic stress resulting in increased energy expenditure (Lata et al., 2015; Daymont et al., 2013; Knirsch et al., 2010; Wheat, 2002; Varan et al., 1999). The finding in the current study are consistent with the findings of Al-Asy et al. (2014), Daymont et al. (2013), Irving, (2011) and Varan et al. (1999) that the extent of the malnutrition is related to the characteristics of the CHD, including the presence of cyanosis. Daymont et al. (2013) found that children with severe CHD showed large, early, and sustained decreases in growth trajectories. Costello et al. (2015) however found no relationship between cyanotic CHD and growth failure prior to cardiac surgery. They suggested the reason for their contradictory findings was that their cohort of children did not include children with severe

forms of CHD such as HLHS. Though the current study had only a single participants with severe CHD, additional factors relating to socioeconomic disadvantage in the current sample are believed to have contributed to the extent of growth failure in both children with cyanotic and acyanotic heart defects.

Post-cardiac intervention growth outcomes tended to remain poorer for children with cyanotic heart defects, especially regarding weight. Both groups however showed significant catch-up growth by the six-month post-cardiac intervention. The largely comparable growth trajectories by six-month post-cardiac intervention is likely due to the fact that most of the children in the current study had moderate (75%) or moderate to severe (20%) disease severity and the majority of the children (75%) in the current study underwent corrective surgery resulting in a considerable improvement in cardiac symptoms.

6.11.2 Developmental outcomes

This study noted no tendency towards different neurodevelopmental outcomes between children with cyanotic heart defects and those with acyanotic defects. Brosig Soto et al. (2011) similarly noted no significant differences in developmental outcomes between cyanotic and acyanotic heart defects. Lata et al. (2015) contradicted these findings by reporting a higher occurrence of developmental delays in children with cyanotic heart defects. The contradictory findings are likely to be explained by the different patient profiles of the respective studies. Half of the children in Lata et al.'s (2015) study had severe disease, whilst only 28.4% of the children in Brosig Soto et al.'s (2011) study had severe disease, compared to only 2.5% of children in the current study having severe disease. This would possibly explain why Lata et al. (2015) found that children with more complex cyanotic heart defects had poorer developmental outcomes.

6.11.3 Parents' perception of health-related quality of life outcomes

In the current study HRQOL outcomes tended to be similar for the children with cyanotic and acyanotic heart defects, with relatively good HRQOL being experienced by the children in both groups. This is consistent with the findings of Hövels-Gürich et al. (2007). This however, contradicts the findings of Mellion et al. (2014) and Schaefer et al. (2013) that more severe CHD and cyanotic lesions are associated with worse HRQOL outcomes. The

reason for these differences can likely be attributed to the difference in the patient profiles of the respective studies.

6.11.4 Parenting stress outcomes

Parenting stress tended to be similar for the parents of the children with cyanotic and acyanotic heart defects in the current study. This is likely due to the fact that patient characteristics were similar for both groups, and the disease severity was only marginally worse in the cyanotic group. No specific reference is made in the published literature to the effect of cyanotic heart defects per se on parenting stress. If the severity of the cardiac disease is used as a proxy for cyanosis the outcomes in the literature are contradictory (Refer to section 6.9.5). It is reasonable to draw this conclusion, as cyanotic heart defects are likely to be more severe.

6.12 Strengths of this study

The current study has several strengths, not only within the South African and African context, but also within the context of global CHD outcome-based research. It must be emphasised that this was a single-centre study and that the findings are relevant to and representative of the population of young children with CHD living in central SA. The findings of this study may however not be generalizable to the entire population of young children living with CHD in SA or on the African continent. Findings may also not be generalizable to young children living with CHD in developed countries.

Perhaps the most important strength of this study lies in the fact that it is the first study in SA, and on the African continent, to have determined the developmental outcome of young children with CHD undergoing cardiac intervention. It is also the first neurodevelopmental outcome study in children with CHD where the majority of the sample consisted of black African children. The majority of participants in the neurodevelopmental outcome studies done in developed countries were white. This is the first study in SA, and one of only a few studies on the African continent to have established the growth and parenting stress outcomes of young children with CHD who have undergone cardiac intervention. This is also

the first study on the African continent to have established the HRQOL outcomes in young children with CHD.

This study included the entire spectrum of children with CHD who would require cardiac neurodevelopmental follow-up, including children with DS. This is also the first study in SA and in Africa to describe the outcomes of children with CHD who also have DS. This study adds to the global body of very limited data on the neurodevelopmental, growth, HRQOL and parenting stress outcomes of children with DS who also have CHD.

This is the first study to provide a detailed description of the rationale behind and development of a home-based parent-driven developmental stimulation programme aimed at addressing the developmental needs, not only of children with CHD in SA, but of children worldwide. The complete programme has been compiled, presented and is ready for further testing and validation.

Furthermore, this study contributes to the limited body of global data on developmental outcomes for children with CHD using the BSID-III. It is the first study to report on HRQOL outcomes for children with CHD using the infant modules of the PedsQL™.

In addition, this study continues to add to the global body of data on the growth, development, HRQOL and parenting stress outcomes for children with CHD. This study is one of only three studies to have reported on neurodevelopmental outcomes prior to cardiac intervention, allowing for comparison of developmental outcomes before and after cardiac intervention.

6.13 Challenges encountered during the study

6.13.1 Logistical challenges

Several logistical challenges were encountered during this study, and were discussed in detail under the pilot study (Refer to section 3.5). Following the pilot study several additional measures were put in place to limit study attrition. These measures where highlighted under section 4.7.

There were a number of logistical challenges experienced prior to cardiac intervention. These included establishing a consistent referral system in the absence of routine cardiac neurodevelopmental follow-up, adapting to changes and cancellations in the cardiac surgery list. A further challenge was completing the baseline assessments the day before cardiac intervention amidst routine medical procedures and investigations, and finding a designated private area in a busy ward to conduct the assessments. The aforementioned could possibly have influenced the child's developmental performance during testing. Assessing parent stress just before their child undergoes cardiac surgery is likely to be reflected in the parents stress scores at baseline. The considerable stress experienced by parents just before their child's cardiac surgery may also have influenced their perception of their child HRQOL at this time point. Findings of this study at baseline needs to be interpreted taking this consideration. It would have been preferable to have done an earlier baseline assessment at another routine hospital visit but in the context of the study site this option was unfeasible.

There were also logistical challenges faced post-cardiac intervention at the follow-up visits. These included not being able to assess the children in the cardiology out-patient clinic due to space constraints, children missing scheduled appointments due to irregular inter-hospital transport and financial challenges on the part of the parents, and children arriving late for their appointments and having to wait until their cardiology follow-up was complete before being able to perform the assessments which resulted in some of them being irritable while being assessment.

6.13.2 Loss to follow-up

Retaining participants in the current longitudinal clinical follow-up study in SA posed difficult, despite concerted efforts to encourage adherence through parent education, SMS text messages and verbal telephonic reminders, and the reimbursement of travelling expenses. Attrition was discussed at length under section 6.1.

Factors contributing to loss to follow-up in the current study included distance to follow-up, unreliable inter-hospital transport services, and socioeconomic disadvantage. Additionally a lack of understanding on the part of the parents regarding the importance of cardiac neurodevelopmental follow-up, even if their children were doing well post-cardiac

intervention, may have contributed to the loss to follow-up. The six-month study visit failed to coincide with a routine cardiology visit, and attendance would have required special effort on the part of the families.

Contacting families to confirm appointments via distance communication methods, including cellular phone calls and SMS text messages, was problematic due to unreliable network coverage in rural areas, the frequent changing of cellular phone numbers, and the inability of parents to afford airtime.

6.13.3 Assessment measures

In regards to the assessment measures, parents lacked confidence in completing the PedsQL™ and PSI-SF unaccompanied, resulting in these measures taking longer than initially anticipated to complete, especially when a translator was required. This perhaps also served as reflection of the low level of maternal education identified in this study.

The BSID-III test items were not found to always be culturally sensitive, despite the reported use of the BSID-III for developmental assessments in SA. The BSID-III contains test items that proved unfamiliar to children living in rural areas and who did not have access to educational toys and storybooks. The standardised storybook item in the BSID-III was in English, yet the home language of the majority of the children in this study was Sesotho. The children's lack of familiarity with several of the test items may have been a reflection on the social disadvantage faced by many South African families that could have resulted in a lack of receptive parenting and suitable age-appropriate stimulation being provided within the home.

Several parents seemed confused by the PSI-SF question six "I am unhappy with the last purchase of clothing I made for myself". The confusion was likely caused by mothers not being able to afford new clothing items due to their low SES. Question 33 also caused confusion, "Think carefully and count the number of things that your child does to bother you". The answer options state "1-3" things as the lowest score-option and does not provide the option of zero. Scoring posed problematic as some caregivers felt their child did nothing

that bothered them. Other parents were unsure of how to count items that bothered them. These two questions of the PSI-SF had to be carefully explained to a number of parents.

In some cases, it was difficult to build a comprehensive picture of the SES of families beyond the primary caregiver, which in most cases was the mother. On completing the Hollingshead Socioeconomic Index, mothers could not always provide as comprehensive a picture of the father's educational attainment and occupational prestige as would have been liked. This was partly due to the fact that fathers were not present at the assessments and, in some cases, were uninvolved in the child's care.

6.14 Study limitations

The results of the current study need to be interpreted against the background of several limitations. This study represents the outcomes of a single cardiac-centre in SA making the results specific to this study population. This means that the findings from this study may not be generalizable to the entire population of children with CHD and their parents as a whole.

There was a high attrition rate in this study, and the limited number of participants available for evaluation at both three-month and six-month post-cardiac intervention may have influenced the analysis of variance findings used to determine associations between multiple variables and developmental, HRQOL and parenting stress outcomes.

The study was also limited by a small sample size. Although the sample was small, it was considered to be representative of the population of young children with CHD served by the Cardiac Unit at Universitas Academic Hospital. Subgroups were small and were inadequately powered to draw definite conclusions on between group differences.

Due to the study methodology, neonates, children who were critically ill and those who had undergone previous or emergency cardiac surgery were excluded from the study sample. This excluded some children with more severe cardiac disease from the study sample.

Despite the AHA's recommendation of the BSID-III as the outcome measure of choice for developmental assessment in children with CHD younger than 42 months, it needs to be considered that it may have potentially underestimated the prevalence and severity of the developmental delays in this population. It is therefore recommend that BSID-III scores be interpreted cautiously in this high-risk population.

Only a disease-specific measure was used to determine HRQOL in children older than two years. Despite HRQOL outcomes being comparable between disease specific and generic HRQOL modules of the PedsQL™ it would be advisable to use a generic module, in combination with a disease-specific measure in future studies, to make comparisons easier with same-aged healthy peers and children with other health conditions. It is also unfortunate that there is no cardiac disease-specific measure available for use when assessing HRQOL in children younger than two years.

The researcher performing the developmental assessments at all time points had the potential to introduced bias.

6.15 Clinical recommendations

Clinical recommendations will be made based on the four key outcomes of the study. Relevant suggestions will be provided for each of the outcomes in the following section.

Growth

The monitoring of growth is particularly important in young children with CHD considering they are at high risk of growth failure, as is evident in this study. A diagnosis of CHD warrants the regular and careful monitoring of all growth parameters, including weight, height, and head circumference, to help identify children at risk of or presenting with suboptimal growth. When indicated, children should be referred to a dietician who can implement strategies to limit growth failure and enhance catch-up growth post-cardiac intervention. A number of parents reported feeding difficulties in the current study. It is therefore also recommended that feeding skills be closely monitored and assessed by a speech therapist when indicated, and suitable therapy initiated if needed.

Development

Young children with CHD are at high risk of developmental delays across all developmental domains, as is evident in this study. It is therefore a strong recommendation that routine cardiac neurodevelopmental follow-up be integrated into standard cardiac care in SA. It is further recommended that clinicians implement the AHA (Marino, 2012) developmental screening and evaluation guidelines for children CHD. There is an urgent need to mobilise awareness and initiate dialogue amongst cardiac services in SA regarding the importance of collaborating with allied health professionals to establish CNP programmes within the country's cardiac units, despite the considerable human resource and financial constraints.

Children identified as being at risk or those presenting with developmental delays should be referred to appropriate EI services, and families should be assisted in accessing these services in order to optimise functional ability and participation of the child within the home and community. In the light of the challenges faced in adhering to hospital-based EI services in SA, it is recommended that innovative strategies be explored to provide early developmental stimulation within the home and in the community. Such innovations would include the implementation of a home-based parent-driven developmental stimulation programme (see Chapter 7). In the current setting it is recommended that parents be provided with an education session and be issued with the programme during their hospital stay post-cardiac intervention as this is the only certain point of contact based on the poor adherence of follow-up appointments.

In this study, several parents reported inattention and hyperactivity in children older than two years. Therefore, it would be recommended that children in this population be monitored for attention-deficits, hyperactivity, autistic spectrum disorders and behavioural problems as they enter their preschool and school years.

The tendency of children with CHD with DS to have considerably poorer developmental outcomes warrants that children who present with CHD with DS be specifically targeted for regular neurodevelopmental follow-up and intensive EI therapy in order to optimise developmental outcomes in this subgroup of children with CHD.

Health-related quality of life

Although the HRQOL of the children in this study was good, it is recommended that HRQOL be established for all children with CHD as part of standard cardiac care and holistic patient management, taking into consideration the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) framework. Mechanisms need to be put in place in cardiac units in SA to provide adequate psychosocial and developmental support to children with CHD so as to optimise their HRQOL.

Parenting stress

Regular routine screening of families for risk of psychosocial morbidity across the cardiac care continuum will assist in identifying families who would benefit from both psychological and education interventions. It is recommended that cardiac parent support groups be established, as they could prove beneficial in providing emotional support to these parents and assist in mediating parenting stress.

6.16 Research implications

Moving past the goalpost of survival, and attending to the promotion of optimal outcomes in at-risk children with CHD and their families, it is of critical importance that studies with larger samples (through multicentre research collaborations) and long-term follow-up be conducted so as to identify ways in which to best assist these children and their families. Against the aforementioned background ssuggestions for further research is provided in the following section for each of the key areas of focus.

Growth

Based on the high prevalence and the extent of the growth failure identified in children in this study, further research is needed to further investigate the growth outcomes of children with CHD more comprehensively over time. Research is also needed to determine the prevalence and nature of feeding difficulties in this population.

The best ways of providing appropriate nutritional support, in conjunction with medical care, for children with CHD in resource-poor settings needs investigation. The effectiveness of feeding interventions, including growth monitoring, nutritional advice, and nutritional supplementation, will need to be established.

Neurodevelopment

Further collaborative research is necessary to establish the developmental outcome of children serviced by cardiac units across SA.

Further research is also indicated to more comprehensively investigate the combined impact of CHD and DS in a larger sample of children.

Considering the high burden of HIV in sub-Saharan Africa it is important for clinicians to keep record of the HIV status of all children with CHD, including those children who are HIV infected, HIV exposed but uninfected and those HIV unexposed, to allow future studies to investigate the neurodevelopmental outcomes for these subgroups of the children.

The developmental screening, evaluation and referral practices of clinicians treating children with CHD in SA (including paediatricians, cardiologists and cardiothoracic surgeons) needs to be determined, as does their awareness of- and implementation of the AHA developmental evaluation and management guidelines for children with CHD.

In addition, further research is required to determine the most appropriate cardiac neurodevelopmental follow-up programme model for implementation in resource-constrained settings, such as SA. The feasibility of running cardiac neurodevelopmental follow-up programmes in SA, and their ability to identify and refer children in need of developmental support, needs to be investigated.

Based on the preliminary findings of this study, research also needs to be done to identify the specific EI service requirements of children with CHD in SA.

Furthermore, research is needed regarding the feasibility and suitability of implementing the home-based parent-driven developmental stimulation programme as an innovative alternative for the provision of early developmental intervention in children with CHD in a geographically challenged and resource-constrained environment.

A suitable developmental screening tool for use in a busy clinical setting in SA also needs to be identified and tested in children with CHD to evaluate its effectiveness in identifying children with CHD who are at risk of developmental delay, and who are in need of more comprehensive developmental assessment.

It is further suggested that children in this sample be followed up into their preschool and school-going years as part of longitudinal research into outcomes in this population.

Health-related Quality of Life

Further qualitative research is recommended to explore in more detail and depth the perceptions of parents of their children's HRQOL and the physical and psychosocial factors affecting HRQOL.

Longitudinal research is also needed to establish changes in HRQOL over time and with the changing developmental age of the child. In older children, child self-reported and parent and healthcare practitioner reported HRQOL outcomes should be compared and seen in combination to provide a complete picture.

In addition, suitable interventions need to be identified and explored that will enhance the health and wellbeing of children with CHD.

Parenting stress

Studying parenting stress outcomes is complex, as there are multiple factors that may influence individual stress outcomes. Factors that need to be taken into consideration include a genetic predisposition to anxiety and depression, personality and temperament, life stressors in play at the time and resiliency factors. Identifying specific factors that impact

on individual parenting stress outcomes will require testing in a larger sample using multiple methods of data collection. It would be recommended that when investigating parenting stress both self-administered questionnaires and semi-structure interviews (qualitative) be included to adequately explore the factors influencing parenting stress.

Research is required to investigate the stress experienced by parents in the cardiac ICU, identifying the stressors at play in this environment.

In addition, longitudinal research is needed in SA to establish changes in parenting stress over time and with the changing developmental age of the child.

Further research is also necessary to determine the true impact of social disadvantage, including variables such as SES and level of parent education on resilience and the ability of parents to cope with caring for a child with CHD in SA.

Additional research is required to determine the effect of educational interventions in reducing parenting stress.

Further research is also needed to determine the effectiveness of cardiac parent support groups in mediating parenting stress in parents of children with CHD.

16.17 Conclusion

The majority of the children in the current study had acyanotic heart disease and most of the children had moderate disease severity. Most of the families were from a low socioeconomic class and the parents had low levels of education. This is in contrast with most of the outcome studies done in developed countries where many more children in the cohorts studied had cyanotic heart defects and severe cardiac disease, including HLHS. Most families represented in studies performed in developed countries were from middle class socioeconomic backgrounds and parents were better educated. Differences in patient and family profiles, as well as methodological differences and varying outcome measures used, largely accounted for the difference in findings. However, it is encouraging to note that

the surgical outcomes of children in the current study were comparable with those in developed countries.

Suboptimal growth was prevalent in the majority of the children in the current study prior to cardiac surgery. The children with cyanotic disease tended to have poorer growth both prior to and after cardiac intervention due to poor feeding and increased metabolic demands. Growth retardation prior to cardiac intervention was also associated with poorer motor development prior to cardiac surgery due to lack of energy, and secondary muscle weakness and hypotonia preventing them from engaging in typical age-related physical activities. The extent of the growth retardation in the current study was greater than that reported for children in developed countries, but similar to reports for developing countries. Growth retardation in children with CHD in developing countries is likely to be exacerbated by poverty and possible HIV co-infection. Consistent with the literature significant catch-up growth for both weight and head circumference took place in the children in the current study after cardiac intervention, but complete catch up growth had not yet occurred by the six-month post-cardiac intervention. The growth trajectories for the children with DS were similar to the children without DS.

The developmental profile and prevalence of developmental delays in the current study was comparable to those of children with CHD in developed countries. Consistent with the literature, motor development was the area of development most affected in younger children before cardiac intervention in the current study. Motor outcomes improved post-cardiac intervention and with increasing age. Cognitive and language development declined with increasing age and skill complexity. The presence of DS was consistently associated with poorer developmental outcomes across all developmental domains. The developmental outcomes of the children with cyanotic and acyanotic heart defects were similar, most likely due to the moderate severity of most of the cyanotic heart defects in the current study. Despite the majority of the children in the current study having moderate disease severity, the extent of developmental delays was found to be greater. It is probable that social disadvantage exacerbated the extent of the developmental delays in the current study. The lack of significant changes in developmental outcome over the duration of the study can be attributed to the low average trajectories that characterise development in children with CHD, and the relatively short duration of follow-up.

The parents in the current study perceived their children as having a good QOL, comparable to their same-aged healthy peers. The children with cyanotic and acyanotic heart defects had a similar HRQOL, likely due to the fact that most of the cyanotic defects included in the current study were moderate in nature. Children with DS however tended to have a poorer HRQOL than the children without DS. Motor development was significantly associated with HRQOL prior to cardiac intervention in the current study. Physical activity limitations and delayed motor skill acquisition were likely to influence the parents' perceptions of their child's HRQOL. Parenting stress was also significantly associated with HRQOL prior to cardiac intervention. Parents' perception of their child's developmental status and general health was likely to have influenced their perception of their child's HRQOL. In the current study, there was a significant improvement in parental perception of their child's HRQOL at three-month post-cardiac intervention, which remained relatively consistent at six-month post-cardiac intervention. This is comparable to the findings in the literature. Improved perception of their children's HRQOL is likely due to the resolution or improvement in the child's cardiac symptoms and their improved physical abilities. HRQOL outcomes for the children with cyanotic and acyanotic disease were similar, because most cyanotic defects in the current study were not severe. The children with DS tended toward poorer HRQOL outcomes than the children without DS.

The majority of parents in the current study reported clinically significant levels of stress in the period immediately before cardiac intervention, and found the surgery and ICU stay particularly stressful. This is consistent with the literature. Even though parenting stress declined significantly at both three-month and six-month post-cardiac intervention, a number of parents continued to experience clinically significant stress. Consistent with the literature, mothers in the current study reported a high burden of care prior to cardiac intervention and financial problems aggravated the stress they already experienced in their parenting role. Perceived HRQOL before cardiac intervention, language development, age of the mother, and age at surgery were significantly associated with levels of parenting stress.

The developmental findings were used to develop a home-based parent-driven developmental activity programme to meet the developmental needs identified from the results of the study presented in Chapter five and the discussion of the findings in Chapter six. The development of the home-based developmental activity programme will be

presented in Chapter seven. The final conclusions drawn from this study will be presented in Chapter eight.

CHAPTER 7

DEVELOPMENT OF A HOME-BASED DEVELOPMENTAL ACTIVITY PROGRAMME (PHASE III)

This chapter describes the processes involved in the development of a home-based developmental activity programme and the supplemental information document. Results indicating the nature of the developmental delay in the current study population will also be highlighted.

This chapter is divided into two sections. In Section I, relevant literature on early developmental intervention programmes and home programmes implemented in paediatric populations at risk of or who present with developmental delay will be presented in support of the rationale behind the design, development, content and proposed implementation of the programme developed as part of Phase III of this study. Early developmental intervention programmes and cardiac rehabilitation programmes conducted in young children with CHD will be reviewed to determine the feasibility of such programmes in this population.

Section II will present Phase III of this research study. Development of the programme took place within the context of two important theoretical frameworks applied widely in paediatric therapeutic clinical practice, namely family-centred care and the International Classification of Functioning, Disability and Health (ICF). A detailed description of the rationale, design and content of the developmental home activity programme and supplemental information document will be presented. The methods employed to validate the content of the home-based developmental activity programme via an expert panel of experienced EI therapists and a focus group of selected parents who participated in the current study will be outlined. Key findings from the expert panel and focus group will be highlighted, and the final home-based developmental activity programme and information document will be presented.

7.1 Introduction

It is well established that children with CHD are at risk of developmental delay. Prospective longitudinal research studies have demonstrated that this risk does in fact become a reality (Long et al., 2015). The patterns of development in the young children with CHD included in this study are in keeping with the patterns of development described in global scientific literature in that motor delays are most common in young children with CHD (Long et al., 2015; Mussatto et al., 2014; Long et al., 2012a; Snookes et al., 2010), and that language and cognitive deficits emerge over time and with increasing age (Mussatto et al., 2014; Long et al., 2012a; Brosig Soto et al., 2011). Developmental delay was also greater in children with genetic abnormalities, including DS (Alsaied et al., 2016; Mussatto et al., 2014; Brosig Soto et al., 2011; Visootsak et al., 2011).

Developmental outcomes in the current study sample affirms the view that neurodevelopmental follow-up and early therapeutic intervention need to be incorporated into routine cardiac care in SA, as in developed countries, in order to optimise developmental outcome and the HRQOL of young children living with CHD. How best to implement developmental follow-up and intervention in the cardiac population in SA is yet to be determined. Limited human resources within the healthcare sector and the social disadvantage faced by many families living in the country need to be taken into account in the design, content and mode of delivery of developmental intervention programmes, if such programmes are in any way to be feasible (Potterton et al., 2010).

7.2 Literature Review

7.2.1 Theoretical frameworks

Family-centred care and the International Classification of Functioning, Disability and Health (ICF) are theoretical frameworks that are widely applied in paediatric clinical therapeutic practice. Family-centred care used in combination with the ICF serves to identify the dimensions of health and wellbeing that should be addressed in early developmental intervention. Both frameworks provide valuable insights into the design and content of early developmental intervention programmes, where there is a focus on enhancing activity and

participation, as well as the facilitation of environmental modifications. In addition, these frameworks support the rationale of why home programmes are considered a desirable means of providing therapeutic intervention (Novak and Cusick, 2006).

7.2.1.1 Family-centred care

Family-centred care is an approach that follows the philosophy that the family plays an imperative role in the health and wellbeing of its members. Family-centred care serves to empower the family to be able to participate in the planning, delivery and evaluation of healthcare services provided to their child (Spearing, 2015; Novak and Cusick, 2006).

In a family-centred approach, parents are viewed as experts in determining the needs of their child (Novak et al., 2007; Novak and Cusick, 2006). As the child lives at home in the care of their family, intervention should be planned and designed in partnership with parents in order to reflect the individual family's priorities (Novak and Cusick, 2006). In clinical practice, this would imply that parents have the right to define the priorities for therapeutic intervention and, in collaboration with the therapist, help direct and implement the intervention so that services meet the family's needs (Novak and Cusick, 2006). Today the involvement of parents in the provision of EI services, including home programmes, is considered to be critical to the success of these services (Novak et al., 2007; Novak and Cusick, 2006; Blauw-Hospers et al., 2011). Home programmes are routinely used as part of family-centred practice as they inherently recognise the expert caregiving abilities of the family (Novak and Cusick, 2006).

7.2.1.2 International Classification of Functioning, Disability and Health (ICF)

The World Health Organisation (2001) developed the International Classification of Functioning, Disability and Health (ICF) in order to provide a scientific basis for understanding health and health-related states (Palisano et al., 2012; WHO, 2001). The ICF serves to define components of health, as well as health-related aspects such as wellbeing (Versaw-Barnes and Wood, 2015; WHO, 2001).

The ICF-CY version is derived from the ICF (WHO, 2001). It was designed with the purpose of better describing the characteristics of the developing child relevant to aspects of health and functioning (WHO, 2007). The ICF-CY includes the same content as the ICF, but has additional content covering the developmental characteristics of children from birth up to 18 years (WHO, 2007). The domains contained within the ICF and ICF-CY include body functions and structures, activities and participation (Versaw-Barnes and Wood, 2015; Palisano et al., 2012; WHO, 2007; WHO, 2001). The WHO model also takes contextual factors into account, including the interaction between the three components of the ICF and the child's own environmental and personal factors (Versaw-Barnes and Wood, 2015; Palisano et al., 2012).

Figure 7.1 provides a schematic representation of the ICF-CY model (WHO, 2007).

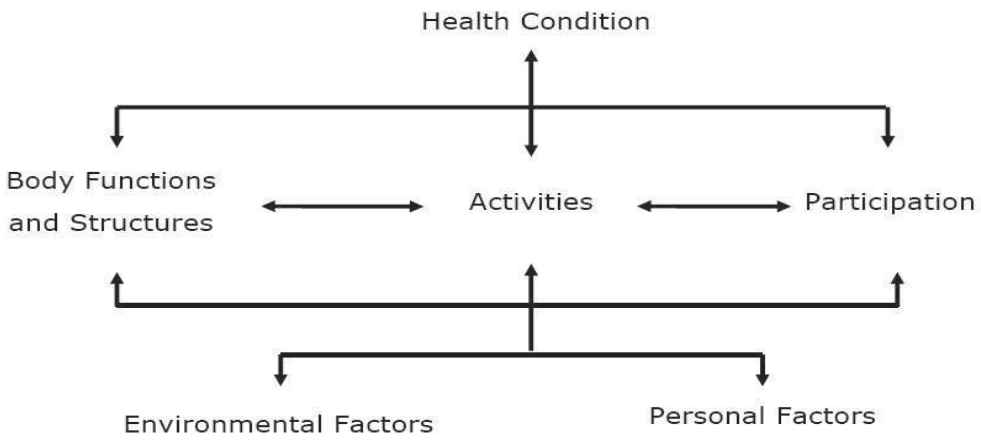

Figure 7.1 The ICF-CY model (WHO, 2007).

To provide a practical example, when applying the ICF framework in the young child living with CHD, it could be postulated that the child could present with various impairments of body function and structure, including musculoskeletal impairments (muscle weakness), cardiopulmonary impairments (poor cardiac function, exercise intolerance and recurrent respiratory tract infections), neuromuscular impairments (low muscle tone, poor motor control and poor coordination), and pain. Activity limitations could include delayed milestone achievement and poor endurance during physical activity. Participation will reflect how the above-mentioned impairments of body structure and function, as well as the activity

limitations, affect the child's participation at home during daily activities or during play (Gocha-Marchese, 2015). Participation in life situations in turn is considered an important aspect of HRQOL (Palisano et al., 2012). In addition, childhood development is a dynamic process and the functioning of the child is dependent on the continued interaction with family and other caregivers. Therefore, the functioning of the child cannot be seen in isolation, but rather in the context of the family system. Family interactions, as well as the quality of the social and physical environment are considered to have a significant impact on childhood development (WHO, 2007). The environment and quality of stimulation can be influenced through early developmental intervention and home programmes (Versaw-Barnes and Wood, 2015; Novak and Cusick, 2006).

7.2.2 Early developmental intervention

Childhood development is an important determinant of health across the lifespan, and early developmental opportunities create a critical foundation for a child's later academic success and general wellbeing (Anderson et al., 2003). The term "early developmental intervention" refers to educational and neuroprotective strategies that aim to enhance brain development and optimise developmental and functional outcome. Early educational strategies seek to take advantage of cerebral plasticity, while neuroprotective strategies include interventions that promote typical development and prevent disability. Neuroprotective strategies would include therapeutic intervention and environmental modifications that aim to provide early, appropriate developmental stimulation (Bonnier, 2008; Spittle et al., 2007). It is generally accepted that early developmental intervention programmes should be initiated during the first year of life, and may continue through toddlerhood and the preschool years (Spittle et al., 2007).

Initially, early developmental intervention programmes were developed for children at risk of developmental delays. These included children at high developmental risk because of poverty, children with disorders associated with developmental delay including DS and cerebral palsy, and children at risk as a result of being born preterm or at a low birth weight (Bonnier, 2008). Available scientific literature on EI relates to programmes implemented in the aforementioned populations.

7.2.2.1 Components of early intervention programmes

A problem encountered when reviewing available EI studies is that most studies provide some information on the intervention, but none provide sufficient detail of the intervention to enable replication of the programme (Benzies et al., 2013). Mothers were involved in the delivery of all documented EI programmes by virtue of their role as primary caregiver (Benzies et al., 2013).

Benzies et al. (2013) performed a systematic review of the published literature on early developmental intervention programmes in preterm infants. They aimed to identify key components of EI programmes. From their review, they identified four key components. These were (i) providing support to parents through advice, anticipatory guidance and/or emotional support; (ii) parent education through information, demonstration, discussion, active engagement and feedback from a healthcare professional; (iii) increasing parental awareness of their influence on their child's development, and (iv) the promotion of parental wellbeing. Similarly, Blauw-Hospers et al. (2011) implemented an EI programme that made use of an approach that included family involvement, parental education, therapeutic handling and providing the infant with the opportunity for repeated practice and play.

There is a growing body of evidence that early developmental intervention programmes should be aimed at enhancing the parent-child relationship and the provision of an optimal environment with appropriate stimulation for learning and development. Such programmes will be best suited and most likely to promote motor, cognitive and social development (Colditz et al., 2015; Blauw-Hospers et al., 2011; Bonnier, 2008; Spittle et al., 2007). Parenting practices have been shown to have a significant influence on a child's development (Colditz et al., 2015). Therefore there should be emphasis on parent education regarding developmental milestones and appropriate stimulation, empowering them to support their child's skills development. Play should also form an important part of any early developmental intervention programmes (Colditz et al., 2015; Blauw-Hosper et al., 2011; Spittle et al., 2007).

The content of home-based early developmental intervention programmes should be based on clinical assessment findings (Spittle et al., 2007). Home programmes provided to parents

are to include activities, exercises and suggestions for toys (Spittle et al., 2007). Blauw-Hospers et al. (2011) further advise that the activities provided should challenge the child to the limit of their capabilities, and that development may be best promoted by providing the child with opportunities to explore their environment by means of trial and error practice.

7.2.2.2 Effectiveness of early intervention programmes

Most children at risk of, or presenting with developmental delay are referred to EI services (Spittle et al., 2007), despite the lack of scientific evidence supporting their effectiveness (Blauw-Hospers et al., 2011; Bonnier, 2008; Blauw-Hospers et al., 2007; Spittle et al., 2007). Additional research is required to determine best practice regarding the design, content and implementation of early developmental intervention programmes (Spittle et al., 2007).

Spittle et al. (2007) reviewed the effectiveness of early developmental intervention provided to infants born preterm post-hospital discharge. They found that there was no standardised protocol for the provision of intervention and that the programmes described in the literature varied greatly. There is also a paucity of information on intervention frequency and dosage. It has been suggested that for home-based developmental intervention, the programme should be implemented daily or at least five days per week for at least 20 minutes per day (Spittle et al., 2007). The optimal timing and duration of EI programmes however remains undetermined (Bonnier, 2008).

There are noted challenges in implementing early developmental intervention programmes in at-risk populations. Hospital-based, therapist-driven programmes face challenges relating to the accessibility of the services to families, and the availability of adequate financing and human resources within the healthcare sector to provide therapeutic interventions services (Colditz et al., 2015; Spittle et al., 2007).

7.2.3 Home programmes

Home programmes are therapeutic interventions specifically designed for implementation within the home, and in the context of daily family life. These programmes are driven by and evaluated by families through interactions with therapists (Engle et al., 2007; Novak and

Cusick, 2006). Therapists working in paediatrics often make use of home-based developmental activity programmes to assist parents in caring for children at risk of, or who present with developmental delay. Home-based, parent-driven intervention needs to be considered as a viable alternative to hospital-based therapist-driven intervention, in that it provides the possibility of sustained exposure to intervention at a low cost (Colditz et al., 2015). Home programmes may therefore hold the greatest potential to impact development over the long-term in at-risk populations (McConnell et al., 2014; Spittle et al., 2007; Tétreault et al., 2003).

There are several advantages to implementing home-based programmes. Home programmes are more convenient and offer more flexibility to families (Novak et al., 2009). In addition, home programmes present an attractive option in an overburdened healthcare system with a shortage of therapists and long waiting times to access therapy. It also provides access to intervention for families who cannot access hospital-based, direct interventions due to geographical and financial constraints (Novak et al., 2009; Tétreault et al., 2003).

7.2.3.1 Components of home programmes

Home programmes are widely used, despite the lack of clinical guidelines to inform therapists' decision-making regarding the design, development, implementation and evaluation of these programmes (Novak et al., 2009; Novak and Cusick, 2006). In an attempt to address the lack of directives on home programmes, Novak and Cusick (2006) developed a model for home programmes containing tasks and strategies therapists can employ when developing and implementing home programmes within the context of the ICF and family-centred care. The model includes five phases namely (i) establishing a collaborative relationship with the family, (ii) collaborative goals setting, (iii) development of the home programme, (iv) delivery of the home programme and supporting implementation, and (v) evaluating the effectiveness and outcome of the programme (Novak et al., 2009; Novak and Cusick, 2006).

Home programmes are considered to play a vital role in assisting families in achieving the desired health outcomes for their child (Novak and Cusick, 2006). Therapists serve as expert

partners in home programmes, working with parents to support their child's development. This is achieved by enhancing caregiver competency and providing the necessary knowledge, skills and resources to enable the family to address the child's developmental needs within the context of their daily life and meaningful participation at home, and during daily activities such as bathing, feeding, dressing and play (Potterton et al., 2010; Engle et al., 2007; Novak and Cusick, 2006).

Home programme development should be based on assessment findings and the concerns and priorities identified by the family (Potterton et al., 2010; Novak and Cusick, 2006; Tétreault et al., 2003). Activities contained in home programmes should form part of the daily routine and fit into the family's lifestyle. Activities should preferably be embedded in functional activities and skills. In addition the programme should be flexible, providing alternative activities that provide parents with a variety of activities they could do (Potterton et al., 2010; Novak et al., 2009; Novak and Cusick, 2006; Tétreault et al., 2003). Suggested activities should be playful and easy to do (Potterton et al., 2010; Novak and Cusick, 2006). When prescribing home programmes, parents should also be advised on how to create a stimulating home environment (Tétreault et al., 2003).

Home programmes work best for parents if they are documented. Parents are more likely to engage in the activities at home if they can be referenced. It has been found that written information, supplemented by pictorials work best (Novak and Cusick, 2006). Home programmes should be disseminated in brochure or booklet form and where indicated the programme activities may be demonstrated to enhance execution at home (Novak and Cusick, 2006).

Parents often find it difficult to maintain momentum with home programme implementation over the long-term (Novak, 2011); and adherence to home programmes varies. Adherence may be affected by the burden the intervention places on families with respect to effort and time (Spittle et al., 2007). The literature highlights several other reasons for non-adherence. These reasons include busy family life, family maladjustment to the child's health condition, difficulties within the home situation, tedious activities often contained in home programmes, poor parental perception of the value of the activities contained in home programmes, and difficulties in the parent-child relationship (McConnell et al., 2014; Novak and Cusick, 2006;

Tétreault et al., 2003). Other noted challenges include marital status, family size, SES and the child's age (Tétreault et al., 2003). Even when parents adhere to home activity programmes, it may come at a personal cost. Caring for a child with greater needs is more demanding and time consuming, and home programmes may further contribute to parental strain and fatigue. Therapists need to be cognisant of this when prescribing home programmes to families (McConnell et al., 2014; Tétreault et al., 2003). The families' perception of the value of the home programme will determine whether therapy is viewed as important, and ultimately successful (Novak and Cusick, 2006). Furthermore, parents' satisfaction with the programme provided to them also affects adherence (Spittle et al., 2007). Providing parents with an appropriate home programme has been found to increase parents' satisfaction with therapy services (Novak et al., 2009).

7.2.3.2 Effectiveness of home programmes

There is overwhelming support for home programmes, and their importance is well recognised; however, their effectiveness in improving function and participation has not been proven (Novak and Cusick, 2006; Tétreault et al., 2003). There is also a lack of guidelines to inform therapists of the frequency, intensity and duration of home programme implementation (Novak and Cusick, 2006).

Novak et al. (2009) investigated the implementation of home programmes in children with cerebral palsy and found that median programme implementation time of 15 minutes per session at a frequency of at least four times per week was adequate to bring about improvements in function and participation. Longer periods or ongoing intervention via home programmes are more likely to effect change (Novak et al., 2009). Novak (2011) suggested that interdisciplinary home programmes might be more effective than numerous individual programmes. It would be easier for parents to implement a single integrated programme addressing all the domains of development at home rather than multiple individual programmes provided by several therapists.

Further research is needed into the effectiveness of home programmes. Therapists need to establish more clearly the burden that home programmes place on families in order to adapt programmes to enhance participation, and thus ultimately their effectiveness, but also

promote the wellbeing of the family (Tétreault et al., 2003).

Potterton et al. (2010) investigated the effectiveness of a basic home stimulation programme in improving the developmental outcome of young HIV-infected children in SA. They found that empowering mothers with a basic home stimulation programme had the potential to significantly improve development outcomes.

It has been recommended that adherence to home programmes can be encouraged and monitored via telephone or SMS text message (Novak et al., 2009). Where parents have access to electronic devices and the internet, advanced video technologies such as Skype can be used as a means of evaluating outcome and adapting home programmes (Rhodan, 2013). However, in developing countries where many parents do not have access to such technologies follow-up by telephone or SMS text message is the best available option. Evaluation of the effectiveness and updating of home programmes in developing countries is likely best done in person at appointments that are scheduled to coincide with other hospital-based appointments (Potterton et al., 2010).

7.2.4 Developmental intervention in children with congenital heart disease

To date there has been minimal investigation into the feasibility and effectiveness of early developmental intervention and home programmes in young children living with CHD who are at risk of or who present with developmental delays (Long et al., 2015; Steiber et al., 2012; Brosig Soto et al., 2011). In addition to developmental delay, children with CHD are also known to present with exercise intolerance and decreased physical endurance during activity (Tikkanen et al., 2012). Despite this, there are no available guidelines for cardiac rehabilitation or physical activity prescription in young children with CHD (Tikkanen et al., 2012).

7.2.4.1 Evidence-based approach to developmental intervention in children with congenital heart disease

The specific guideline published by the American Heart Association (2012) targets the early identification and management of developmental delays and disorders in children with CHD,

with the goal of optimising developmental outcome (Marino et al., 2012). The guidelines provided on developmental screening and evaluation are expansive, but there is a lack of information on the management of developmental delays once identified. The guideline simply states that a collaborative interdisciplinary approach should be followed with the referral of the child and family to EI therapy services to address the areas of development in which the child is having difficulty. EI therapy services include PT, ST and OT. No further information is provided on the design, content and dosage of these developmental interventions. The guideline also makes no mention of physical activity prescription or cardiac rehabilitation as part of intervention. Given the possibility that the early appropriate intervention may potentially alter the long-term neurodevelopmental outcome and HRQOL of children living with CHD (Knutson et al., 2016), further clarification on the nature of the intervention is therefore required as part of the management guideline.

7.2.4.2 Early developmental intervention for children with congenital heart disease

Despite evidence regarding the occurrence of neurodevelopmental delays in children with CHD, little research has been done to examine intervention programmes to address these developmental delays (Long et al., 2015; Steiber et al., 2012; Brosig Soto et al., 2011). Both of the documented programmes implemented by Long et al. (2015) and Steiber et al. (2012) failed to follow an interdisciplinary approach and addressed only a single area of development. Both programmes were developed and presented by physiotherapists in an attempt to improve motor development outcomes (Long et al., 2015; Steiber et al., 2012).

Kendall et al. (2003) and Lewin et al. (2002) investigated the extent to which rehabilitation services were provided to young children with CHD in the UK. Eighty-two percent of the participants in their study, who were all healthcare practitioners directly involved in paediatric cardiac care, indicated that there was a need for rehabilitation services. Contrary to the identified need, children's rehabilitation priorities were only discussed by the cardiac team in 41% of cases. Brosig Soto et al. (2011) reported that only 51.6% of children with CHD were referred to EI services. These findings were similar to the referral rates to EI services reported in a study by Hoskoppel et al. (2010). More concerning is that 31% of children meeting the criteria for EI did not receive these services (Brosig Soto et al., 2011).

The timing of initiating intervention in children with CHD proved to be a challenge as noted in the studies by Long et al. (2015), Steiber et al. (2012) and Brosig Soto et al. (2011). The perception of families' of the need for developmental intervention posed a considerable hurdle. Placing a high priority on early therapeutic intervention to address developmental concerns may seem inappropriate to families who are to face or have just faced a major cardiac surgery or even a life-and-death situation. As children recover post-intervention and do better, parents may feel that there is no longer any need for developmental intervention. This may contribute to families failing to access EI services despite referral. The aforementioned studies however remain unclear on whether the lack of EI services being accessed by families is because of family factors, such as interest and availability of time, or a lack of access to EI services due to human resource and financial constraints within the healthcare sector. According to Long et al. (2015) a large number of families staying a considerable distance from service points are lost to follow-up; and this would also need to be factored into the timing of implementing early developmental intervention in this population.

There are only two reported studies to date that have investigated the feasibility of early developmental intervention in children with CHD. Long et al. (2015) investigated the efficacy of a physiotherapy EI programme on the gross motor development of infants with CHD using both a hospital-based and home-based-intervention approach in Australia. Home-based intervention was provided to participants who resided a considerable distance from the service point; while hospital-based EI appointments were scheduled for local families to coincide with other hospital appointments in an attempt to improve compliance. Intervention was provided on a needs basis. The frequency of the intervention sessions was weekly, bi-weekly or monthly, based on the extent of the developmental delay. The participants who received the home-based intervention were provided with a single physiotherapy session prior to hospital discharge following cardiac intervention. Parents were provided with home-based strategies to address identified gross motor delays. The study intake was stopped after ten months as the hospital-based intervention strategy proved to be infeasible.

Steiber et al. (2012) investigated the feasibility of a ten-week, play-based, parent-delivered home-based EI programme on motor development in children aged 12 to 26 months with CHD in Canada. Play-based activities were individualised in accordance with each child's

developmental age. Two motor development goals were selected as the target activities for each two-week period. For each target activity, the parents were provided with four to six play-based activity options using games and songs. Parents were asked to engage their child in one or more of the options for a total of ten minutes or more each day so that the total intervention time per day was 20 minutes. Adherence to the home-based rehabilitation programme ranged from 0 to 100%, with only two families reporting complete adherence to the prescribed programme.

Long et al. (2015) and Steiber et al. (2012) both noted that the distance parents had to travel to access hospital-based services posed a significant hindrance to the implementation of early developmental intervention programmes. As cardiac surgery is usually performed at a cardiac centre located in a large city, patients often come from a wide geographical catchment area. Long et al. (2015) made the clear determination that hospital-based EI services were impracticable and poorly suited to address the developmental needs of young children with CHD.

The implementation of home-based developmental intervention programmes in young children with CHD is however in itself not without its challenges. When parents within the home setting administer an intervention programme, adherence and the effectiveness of the intervention provided become extremely hard to measure (Steiber et al., 2012).

Family education should be provided as part of EI programmes, and should include information on sternal precautions to be adhered to post-operatively and age-appropriate developmental positioning. The importance of physical activity and early developmental intervention should also be emphasised (Hanson, 2015).

Evidence suggests that the developmental needs of children with CHD are for the most part not being met globally. Convincing both parents and the cardiac community that early therapeutic intervention improves developmental outcome, prevents morbidity and improves HRQOL requires scientific evidence that is not currently available. According to Long et al. (2015) the required evidence can only be gathered through ongoing scientific research where the early developmental intervention programme design, content and method of delivery are well documented. The frequency and dosage of intervention also needs to be

assessed objectively in order to determine the dosage required to bring about changes in developmental outcome. Clinical guidelines for early developmental intervention in young children with CHD can only then be compiled and put into practice (Long et al., 2015).

7.2.4.3 Use of prone positioning as a developmental position in children with congenital heart disease

Play provides a vehicle for exploration of the environment. The child awaiting cardiac surgery often has very little opportunity for play and physical exploration (Hanson, 2015). Despite environmental limitations pre-operatively and post-operatively, children with CHD should be exposed to, and parents should encourage all developmental positions, including prone if tolerated. If not tolerated parents should try to make use of modified prone positioning over a towel roll, cushion or over the mother's shoulder (Hanson, 2015). If children are not regularly placed in prone while awake they may become intolerant of the position (Dudek-Shriber and Zelazny, 2007). Prone is considered an important developmental position as it is considered a forerunner for other developmental positions including crawling and weight bearing on the upper limbs (Du et al., 2015; Hanson, 2015). In addition, prone development has been found to influence milestone achievement in other developmental positions such as supine and sitting (Dudek-Shriber and Zelazny, 2007). Prone is seldom contraindicated in children with CHD, apart from in the immediate post-operative period following a median sternotomy. Parents should be advised to encourage "tummy time" from two weeks after sternal closure, depending on tolerance, with a goal of 40 minutes per day, which can alternatively be broken down into four ten minute sessions (Lucile Packard Children's Hospital, 2015).

7.2.4.4 Physical activity prescription in young children with congenital heart disease

Physical activity is considered a basic requirement for childhood development. Perceptual and motor experiences determine physical and motor development, and also affect emotional, psychosocial and cognitive development (Müller et al., 2013; Bjarnason-Wehrens et al., 2007a). Survivors of CHD often present with comorbidities that impair their physical abilities. On top of physical impairments, development is often negatively impacted by environmental factors, such as parental overprotection, which may further predispose the

child to physical inactivity and exercise intolerance. This may potentially have serious long-term development and HRQOL implications for CHD survivors (Du et al., 2015; Müller et al., 2013; Tikkanen et al., 2012; Bjarnason-Wehrens et al., 2007a).

The impact of parental overprotection on development and physical endurance cannot be underestimated. Parents unnecessarily restrict their child's physical activity, and are often uninformed about the potential benefits of physical activity (Müller et al., 2013; Bjarnason-Wehrens et al., 2007a). Children with CHD require no restriction of physical activity unless there is significant cardiovascular compromise. Therefore, most children with CHD can and should participate in the same physical activities as their same-aged healthy peers (Hanson, 2015; Tikkanen et al., 2012; Bjarnason-Wehrens et al., 2007a).

The benefits of physical activity are not restricted to the cardiovascular system alone, but may also address comorbidities in other systems affected by CHD. Cardiorespiratory complications may limit the capacity for physical activity, but mobilisation and physical activity on the other hand may serve to improve cardiorespiratory function. Increased physical activity may also in turn address neurodevelopmental concerns such as developmental delays, musculoskeletal problems and low muscle tone. A strong relationship exists between muscle strength and physical endurance and exercise tolerance; therefore, improving muscle strength would prove beneficial in improving physical endurance (Hanson, 2015; Riner and Hunt Selhorst, 2013; Tikkanen et al., 2012; Bjarnason-Wehrens et al., 2007a).

One would anticipate that the benefits associated with exercise training in adults with cardiovascular disease would be transferable to even young children with heart disease, but to date there has been limited published research into paediatric cardiac rehabilitation. There is no published research on cardiac rehabilitation and activity prescription in children with CHD under the age of four years. The findings in the few published studies in children aged four years and older strongly support the benefits of incorporating physical activity in rehabilitation programmes for children with CHD (Tikkanen et al., 2012).

There are no clear guidelines available on physical activity prescription in young children with CHD (Du et al., 2015). There is insufficient evidence to recommend formal exercise

programmes in infants and toddlers as a means of increasing physical activity (AAP, 2006). The American Academy of Paediatrics (AAP) (2006) does however encourage parents to provide a safe, nurturing and minimally structured play environment for infants and toddlers. Similarly, Hanson (2015) and Bjarnason-Wehrens et al. (2007a) suggest that parents should allow their toddlers or pre-schoolers with CHD to partake in unrestricted physical activity and participatory activities, such as play to enhance the physical, emotional, psychosocial and cognitive development, ultimately improving their child's HRQOL.

The aforementioned recommendations provided by the American Academy of Paediatrics (2006), Hanson (2015) and Bjarnason-Wehrens et al. (2007a) are very broad, and parents are likely to require more specific instruction regarding physical activity and play to encourage adherence. It would be an oversight not to also consider the application of the FITT (frequency, intensity, type and timing) principles of exercise prescription, as recommended in the American College of Sports Medicine (ACSM) (2006) guideline, when considering the prescription of a home-based developmental activity programme for young children with CHD (Haskell et al., 2007).

The FITT principles are outlined in Figure 7.2.

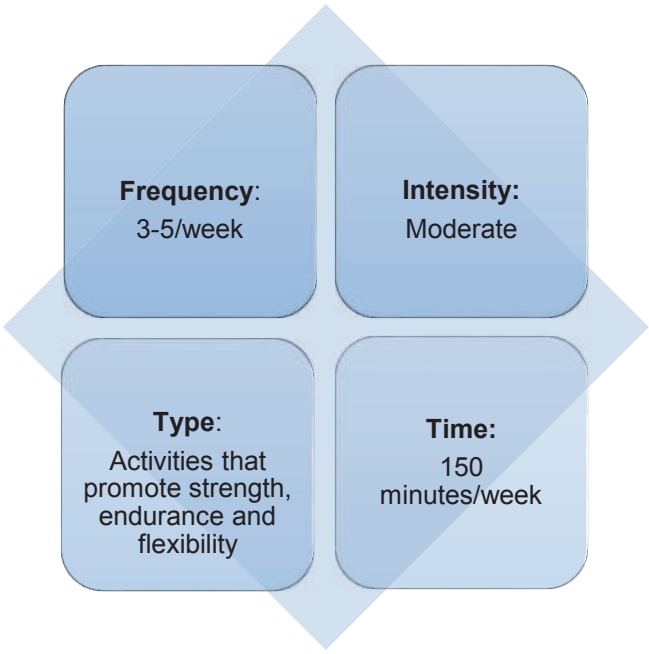

Figure 7.2 FITT principles of exercise prescription (American College of Sports Medicine, 2006)

Applying the FITT principles in physical activity prescription for infants and toddlers with CHD, where physical activity is focused on age-appropriate developmental activities and play, requires some innovative adaptation. The following recommendations can be made, taking into consideration the activity prescription guideline proposed by Du et al. (2015) for their prospective study on exercise intervention (passive movement and active exercise) in infants with CHD.

Frequency

It has been suggested in children aged four years and older that physical activity provided five days a week would suffice in improving physical endurance and exercise tolerance (Du et al., 2015). This is in line with the ACSM guideline (2006), and therefore it could be recommended that young children with CHD should engage in daily physical activity.

Intensity

Though the ACSM guidelines recommend physical activity of moderate intensity, how exactly this translates into dosage in young children is yet unclear. Du et al. (2015) suggested that a short duration, low-dose intervention programme of physical activity as developmentally appropriate as possible, would be best-suited (Du et al., 2015).

Time (duration)

It has been suggested in children aged four years and older that physical activity provided for 25 minutes per day, will suffice in improving endurance and physical activity (Du et al., 2015). This aligns with the suggested 20 minute duration of home-based developmental intervention proposed by Steiber et al. (2012), Novak (2009) and Spittle et al. (2007).

Type

Du et al. (2015) noted that physical activities should include developmental activities that are appropriate for the child's age. This aligns with intervention activities used by Long et al. (2015) and Steiber et al. (2012) as part of EI programmes in children with CHD.

In conclusion, there is a clear need for therapeutic intervention that includes age-appropriate physical activity in order to adequately address physical endurance and exercise intolerance concerns in children with CHD (Hanson, 2015; Tikkanen et al., 2012; Bjarnason-Wehrens et al., 2007a). As evidenced, the use of developmentally appropriate physical activity to improve physical endurance and exercise tolerance in young children with CHD is undervalued and underutilised as part of therapeutic intervention. The best design of physical activity programmes in young children with CHD remains unclear. From a parent-centred care perspective, it is recommended that physical activity programmes be home-based and parent driven (Tikkanen et al., 2012; Bjarnason-Wehrens et al., 2007a; Bjarnason-Wehrens et al., 2007b). As parental fear may be a barrier to children partaking in physical activities (Bjarnason-Wehrens et al., 2007a; Bjarnason-Wehrens et al., 2007b), parent education on the benefits of physical activity and the provision of clear physical activity guidelines are to be considered an important component of home-based developmental activity programmes (Tikkanen et al., 2012).

7.3 Rationale and development of the home-based parent-driven developmental activity programme

7.3.1 Introduction

Scant information is currently available in the literature on parent-driven, home-based EI for young children with CHD. The strongest scientific evidence, as presented above, was used to determine the framework for the development of the home-based developmental activity programme. Long et al. (2015) strongly recommended that future research into home-based developmental intervention in children with CHD should clearly define the design, content, dosage and implementation strategy used so as to determine best practice. In light of this, the process for the development of this home-based developmental intervention will be described comprehensively.

7.3.2 Rationale behind the home-based parent-driven developmental activity programme

In keeping with current best practice evidence, it was decided to develop the programme within the framework of family-centred care and the ICF-CY. Thus it was decided that the programme should be home-based and parent-driven to optimise the child's functional abilities and enhance participation in his/her own home environment and community. Further motivation for designing a home-based, parent-driven programme was the consideration that families face considerable challenges in accessing hospital-based services due to geographical and financial constraints. The aforementioned challenges as relevant to the current study population were discussed in Chapter 6.

There is an extreme shortage of experienced neurodevelopmental therapists throughout the public health sector in the SA. In addition, cardiac centres do not have the funding available to appoint therapists to run CNPs and provide EI therapy services to these children. A community-based service will also likely be impracticable. Community rehabilitation services are understaffed and tend to be provided by recently qualified and inexperienced therapists. Therefore the only practicable option of providing high quality, sustainable, long-term early developmental intervention in this population would be that EI therapy services be initiated at specialist cardiac units by experienced therapists, but be home-based and parent-driven.

After the determination that the best-suited mode of programme delivery would be home-based and parent-driven it was decided that Novak and Cusick's (2006) model for home programmes would serve as a suitable framework from which to develop this programme.

7.3.3 Development of the home-based parent-driven developmental activity programme

The steps taken in the development of this home-based, parent-driven developmental stimulation programme are presented below:

Step1: Establishing a collaborative relationship with key stakeholders

The researcher established a collaborative relationship with the families recruited into the study over the six-month period during which their children were followed-up after cardiac intervention. Parents often provided invaluable insights into their fears, concerns, wishes and needs during these assessments. This anecdotal information proved extremely valuable when determining the format and content of the programme.

Satisfaction regarding the proposed content of the developmental home activity programme was established with key stakeholders, including parents who would have to execute and participate in the programme at home with their child, as well as rehabilitation therapists who would be responsible for providing the programme. This was done via a focus group of parents who took part in this study and an expert panel of rehabilitation therapists working in early childhood development (this included occupational therapists, physiotherapists and speech therapists).

Step 2: Goal Setting

Developmental aspects that would need to be addressed in the programme were identified from the developmental outcomes of the participants in Phase I and Phase II of the current study where cognitive, language and motor performance was determined using the BSID-III. The goal was to develop a single, interdisciplinary programme that would address all developmental domains including cognition, receptive and expressive language and fine and gross motor function. A single interdisciplinary programme allowed for implementation by a single therapist if need be; this taking into consideration the shortage of experienced neurodevelopmental therapists in the country.

The programme had to be suitable for all children with CHD, including those at risk of or presenting with developmental delays. Considering the high loss to follow-up and the large number of parents who are unlikely to access EI services post-intervention, the issuing of this programme prior to discharge would provide parents with a developmental activity guide, which they could reference, and use over time. It would also be suggested that children and their parents be seen as part of a CNP at routine cardiology follow-up visits so that any development concerns can be addressed and the implementation of the developmental activity programme supported.

Step 3: Design and content of the programme

The programme is a home-based parent-driven developmental activity programme.

Parental education is deemed critical to the implementation of the home programme. During this study, several aspects were identified that would need to be addressed as part of parent information in this population. It was identified that parents needed information on the relationship between CHD and developmental risk, developmental milestones, the importance of providing suitable developmental stimulation and encouraging physical activities at home, as well as the importance of adequate nutrition. A number of the children in this study had CHD with DS and parents required additional information on the unique developmental challenges facing their children. Another important gap identified during Phase I of this study was that parents were not being provided with any information regarding sternum precautions, appropriate developmental positioning (especially concerning prone positioning), and activity restriction post-cardiac surgery. In addition, no information was provided on wound care prior to hospital discharge.

The ***content of the home programme*** was based on developmental outcomes and expected developmental skills. Bedford et al. (2013) aptly describes childhood development as a measure of abilities and aptitude, making comparisons with same-aged children. Developmental performance is usually described in terms of the developmental tasks the child can or cannot perform. Based on these grounds, the current EI literature strongly recommends that early developmental intervention and home programme content be based on assessment findings and that the child should be provided the opportunity to master skills

he/she is struggling with (Long et al., 2015; Steiber et al., 2012; Potterton et al., 2010; Spittle et al., 2007; Novak and Cusick, 2006).

From clinical experience, it is to be considered likely that therapists will provide advice and prescribe developmental activities for a home programme based on skills that the child struggled with or could not do during assessment. Aligning an intervention and home programme with the assessment findings provides continuity and increases parental acceptability of the assessment test (Bedford et al., 2013). The age-appropriate developmental skills tested under the various domains of the BSID-III were determined through an extensive literature review process to determine age-expected skills (Bayley, 2006a). The developmental skills contained in the BSID-III are not unique to the BSID-III alone. Similar skills are tested by 13 other developmental outcome measures, which cover all the developmental domains of interest. These measures include the Denver II, Battelle Developmental Inventory Second Edition (BDI-2), Child Development Inventory (CDI), Child Development Review (CDR), Mullen Scales of Early Learning (MSEL), Brigance Early Childhood Screens, Griffiths Mental Development Scales-Extended revised (GMDS-ER), Schedule of Growing Skills-II and the Ages and Stages Questionnaire (ASQ-3). All of these measures assess universal developmental skills across key developmental domains (Bedford et al., 2013).

Thus, the skills identified for age can be considered typical of childhood development and not specific to an individual measure. The BSID-III is viewed as the gold standard measure of development (Bedford et al., 2013; Marino et al., 2012). In the light of its high standing and strong psychometric properties the age expectations for skills development were considered a valid guide.

ADL related to bathing, eating, playing and bedtime were considered important for parents to participate in. Suggestions were also included for age-appropriate toys and low-cost toy options for parents who could not afford expensive educational toys. The programme was to provide parents with a “resource toolbox” of developmental stimulation activities they could do at home. The array of activities offered parents flexibility and a variety of activities that could be changed on a daily basis.

A progressive programme of physical activities would be encouraged to improve physical endurance and exercise tolerance, as appropriate for age. Time for free play would also assist in this regard. The treatment dosage would be aligned with current suggestions for developmental intervention and physical activity prescription in young children. The recommended frequency for implementation of the home programme would be five times a week, with a minimum of at least three times per week. The target duration of the intervention should be at least 20 minutes per day. It would be recommended that the duration of physical activity be progressed incrementally to improve physical endurance and exercise tolerance. The programme would be issued to families in writing, and in colour, using an A5 booklet format. The booklet is supplemented by illustrations of developmental activities. In addition, parents would be provided with a written information document containing relevant parent education information.

7.4 Method for Phase III

Key stakeholders, including parents and rehabilitation therapists, were to be consulted to assess the validity and the suitability of the content of the home-based developmental activity programme that was developed in order to enhance the quality and validity thereof.

7.4.1 Location

The focus group of selected mothers who participated in Phase I and II of this study was held at the Physiotherapy Department at the Universitas Academic Hospital in Bloemfontein. The expert panel members were contacted electronically via e-mail and telephone due to the geographical diversity and busy schedules of the healthcare professionals involved.

7.4.2 Ethical considerations

Ethical clearance was obtained for Phase III of this study (together with Phase I and II) from the Ethics Committee of the Faculty of Health Sciences, University of the Free State (clearance certificate number ECUFS 177/2013) and the Committee for Research on Human Subjects, University of Witwatersrand (clearance certificate number M131056).

Participants in Phase III of this study included a select group of mothers, who participated in Phase I and II, and rehabilitation experts. All participants were informed of the purpose of Phase III of this study by means of an information letter; further verbal explanation was provided by the researcher upon request. Parents provided written informed consent (See Appendix XVIII) before the focus group commenced, and therapists consented to participation by reviewing the home activity programme sent to them electronically and submitting their feedback (See Appendix XIX).

A contribution was made towards the transportation costs incurred by the mothers for their attendance of the focus group. No remuneration was provided to the rehabilitation therapists for their participation. The study was conducted in line with the approved protocol. Participation in this, Phase III of this study, was voluntary. Parents and rehabilitation experts had the right to decline participation or withdraw at any point without reason or risk of penalty.

7.4.3 Study design

Phase III made use of a qualitative study design.

7.4.4 Participants

Phase III of this study consisted of two groups of participants, namely the focus group of mothers and a panel of rehabilitation experts.

7.4.4.1 Focus group

Six mothers, who had exited Phase II of the study, were invited to participate in the focus group to gain consensus on the content of the home developmental activity programme. They were selected due to their personal knowledge of caring for a child living with CHD, and had been through the process of the three developmental assessments on the BSID-III that formed part of Phase I and Phase II of this study.

It was decided that including six mothers in the focus group would be sufficient in the consensus-gaining process on the home-based developmental activity programme in this study. The focus group size was aligned with the group size recommended in the literature. According to Sagoe (2012), Wong (2008), Lakshman et al. (2000) and Kitzinger (1995), a focus group in medical research should typically be between four and 12 people.

Mothers were selected for the focus group if they met the following inclusion criteria:

- Had to have taken part in Phase I and II of the study, and exited the study at the end of Phase II.
- Had to be English literate.
- Resided in and around Bloemfontein and could easily commute to Universitas Academic Hospital for the session.
- Provided written informed consent for their participation in Phase III.
- We're willing and able to attend the scheduled group session.

7.4.4.2 Expert panel

A panel of six rehabilitation experts including physiotherapists, occupational therapists and speech therapists, were selected for their experience in working in early developmental intervention services in SA. Representation of all three of the therapeutic allied health professions was decided upon, based on the multiple domains of development contained in the developmental home activity programme, as well as the goal of the programme being able to be presented in clinical practice by any member of the rehabilitation team.

The following inclusion criteria were applied for the expert panel of rehabilitation therapists:

- Were practising at the time of the study as a physiotherapist, occupational therapist or speech therapist in SA.
- Had neurodevelopmental therapy (NDT) certification as a minimum requirement, but having advanced NDT certification in early intervention was considered beneficial.
- Had at least five years' working experience in early childhood intervention services. Experience working with children with CHD was considered advantageous.
- Provided consent to participate in the expert panel during Phase III of the study by reviewing the programme and submitting feedback.

Due to the qualitative nature of the research, a purposive sampling method was used to identify six rehabilitation experts who met the inclusion criteria. The aim of the expert panel was to gain consensus about the content of the home-based developmental activity programme. It was decided that six rehabilitation experts would be sufficient in the consensus-gaining process on the developmental home activity programme in this study.

The size of the expert panel was within the recommendations provided in the literature. According to Jones and Hunter (1995) it is recommended that a medical expert panel consist of up to a maximum of 12 members. The number of participants in an expert panel to gain consensus varies considerably in medical consensus studies done to date and depends largely on the topic of investigation.

7.5 Procedure for Phase III

Following the final six-month post-cardiac intervention follow-up all developmental assessments on the BSID-III for Phase I and II were scored and the data analysed to establish the prevalence and nature of the developmental problems faced by children with CHD in this sample. It was found that children with CHD presented with developmental delays following the patterns described in chapter 5 (Refer to section 5.7). Motor delays were most prevalent before cardiac intervention and during infancy, and language and cognitive delays became more apparent with age. Children with DS presented with more significant delays in all developmental domains, compared with children with CHD without DS. Developmental outcome findings and a comprehensive literature review were used in the development of the developmental home activity programme, as already described.

Following the compilation of the home-based developmental activity programme, consensus about the content of the programme amongst the key stakeholders was established (CDC, 2006). Key stakeholders were considered to be the rehabilitation professionals who would be providing the programme to families, as well as parents who would be encouraged to participate in the programme at home. Phase III took approximately four months to complete. The focus group and the expert panel ran in parallel.

The procedure for both the focus group and expert panel will be described below:

7.5.1 Focus Group

A focus group discussion is a qualitative research method whereby a small group of participants gather to discuss a specific topic in order to generate data. Characteristic of a focus group is the interaction between the facilitator and the group, as well as the interaction between the group members. The main objective of a focus group is to gain an understanding of the participants' perspective on the topic of discussion (Wong, 2008).

Seven mothers met the aforementioned inclusion criteria, and were identified for potential participation in the focus group. These mothers were contacted via telephone and SMS text message to invite them to participate in the focus group. Two of the mothers were subsequently found to be untraceable at the contact numbers previously provided, despite repeated attempts. Two mothers were unable to attend the scheduled group session as they had subsequently been employed after exiting the study and could not afford to miss a day's work. However, they were willing to review the programme in their own time and provided their input when contacted telephonically afterwards. Three of the mothers contacted were willing to participate in the focus group session.

In an attempt to increase and enhance the quality of the feedback provided by parents from this study, the researcher reviewed the clinic appointments for March 2016 to see if any families who had participated in the study, but resided outside of Bloemfontein, were scheduled for a cardiology follow-up visit. Two mothers were identified and contacted at the clinic, and were willing to review the programme in their own time. They were contacted telephonically for feedback on the programme afterwards.

A date was identified for the focus group and the details were communicated to the three participating parents. They were reminded telephonically and via text message of the session by the researcher three days before the scheduled session and on the day before the session. One of the three mothers who participated in the focus group had a child with DS. The focus group was held in the committee room at the Department of Physiotherapy at Universitas Hospital. This provided comfortable seating and a table at which to write. Refreshments were provided. The researcher served as the facilitator (interviewer) of the

group. At the session, the facilitator explained the aim of the session and orientated the parents in regards to the procedures. Written informed consent was obtained from each participant before starting. Parents were provided with a pen, as well as a copy of the information document (See Appendix XX) and the developmental activity programme (See Appendix XXI) printed in colour and in A5 booklet form. Parents were given 40 minutes to read through and review the documents provided to them. Any additional comments could be noted on the documents with the pen provided. A discussion followed regarding their experiences, as well as the comments and suggestions provided.

Parents were sent home with the home programme and encouraged to think about the document again and were followed up 10 days later to find out if there were any additional comments. Parents who reviewed the programme outside of the group context were contacted via telephone for their input.

7.5.2 Expert Panel

According to Jones and Hunter (1995) the use of an expert panel in medical research is a qualitative method applied in order to gain consensus and synthesise information. An expert panel is to be considered invaluable in areas of medical research where published information is inadequate or not available, providing a method of gaining information and the insights of appropriate experts to enable decision-making. As very little published information is available on the content of developmental home programmes, it proved the most suitable means of gaining consensus on the content of the developmental activity programme.

Two physiotherapists, two occupational therapists and two speech therapists who met the inclusion criteria, were identified and selected for the expert panel. These therapists were contacted via e-mail inviting them to participate in this study. An information letter was included in the e-mail sent out to them. The developmental activity programme was sent to the therapists electronically to review. By reviewing the programme and providing feedback, the expert was agreeing to participate. A clear deadline was provided for submission in all feedback. Reminders were sent out every ten days via e-mail and SMS text message.

7.6 Interpretation of the findings from the focus group and expert panel

7.6.1 Focus group

It proved more logistically challenging than anticipated to get local mothers to attend the focus group, and only three mothers were able to attend. An additional three mothers reviewed the programme independently and provided feedback over the phone. In total, feedback on the home-based developmental activity programme was received from six mothers.

Anecdotal comments provided by parents during Phase I and II of the study were an important consideration in the development of the parent information document and the home-based developmental activity programme. Key areas parents commented on were listed for more in depth discussion during the focus group. These included the need for information on nutrition, developmental milestones, and signs for concern regarding developmental performance, suitable developmental stimulation within the home, and sternum precautions and activity restrictions post-cardiac surgery.

Following the in-depth discussion of the tabled discussion points and their feedback on the home-based activity programme, parents indicated that they were satisfied with the content of the information document and home-based developmental activity programme and suggested no further additions. They indicated that they felt it would be important that these documents be issued on admission, as this would allow sufficient time for parents to read through them and ask questions before being discharged home. They were also of the opinion that an information session with the therapist to discuss the programme prior to discharge would be beneficial in encouraging adherence. They reported finding the precautions and activity limitation guidelines particularly important to have explained to them before discharge, as they were unsure of any precautions that needed to be applied.

Parents felt the milestones as documented in the developmental activity programme were easy to read and understand. They particularly liked the activities that incorporated play and daily activities, and felt that the activities would be doable in their daily routine. The mothers also approved of the toy adaptations for low-income situations and found the advice

regarding toys to be important. They thought it feasible to issue the developmental activity programme in a two-hour education session post-cardiac intervention, but prior to discharge. The majority of the mothers were also of the opinion that they would like to have developmental activities explained to them, and where necessary, demonstrated. They also suggested that parents should be informed to come in earlier on the day of admission for cardiac surgery so that routine developmental assessment could be done in the morning before the child was admitted to the ward.

Additional issues that came out in the discussion that were of importance included parents being satisfied with the information provided by the cardiac surgeon regarding the surgery beforehand, however all of them felt completely unprepared for seeing their child in the cardiac ICU. They found the experience was overwhelming and incredibly stressful. They voiced the need for better orientation to the cardiac ICU beforehand and the need to be informed about the drains, endotracheal tube and indwelling devices. Their child's discomfort and pain was hard for them to witness, and they felt unable to care for or comfort their child in that situation.

Parents' valued the regular developmental assessments and follow-up. They felt that it reinforced that their children were progressing well, and allowed for questions and advice. They also indicated that they were in favour of the fact that that advice provided on developmental stimulation was aligned with the items that were tested during the developmental assessments.

Parents indicated that they experienced very high levels of stress after their child's CHD diagnosis. This stress was exacerbated by their experiences in the healthcare system. They viewed the most stressful time as being the period being just before cardiac surgery and when their child was in the cardiac ICU. All the parents were of the opinion that they would have benefited from additional psychological support and counselling during this period, in particular. They felt that the study follow-up visits provided additional support to them, and they enjoyed the regular sessions. They expressed the need for their children's development to be followed up over the long-term. They were also of the opinion that the SMS text message reminders for follow-up appointments contributed to their adherence.

The mothers unanimously motivated for the establishment of a support group for parents of children with CHD at the Cardiac Unit at Universitas Academic Hospital. They were of the opinion that parents going through the same experiences could share their experiences, and that they could support each other. Mothers whose children had already been through cardiac surgery could provide valuable insights to other parents regarding their lived experiences.

7.6.2 Expert panel

All the therapists were pleased with the home-based developmental activity programme provided to them for review, and were of the opinion that it would be a valuable resource tool for families in the SA context. There were several comments made by the therapists that were carefully considered and weighed-up, where appropriate, minor amendments were made to the programme. The comments provided by panel members deemed to be important, will be discussed hereafter.

A single therapist noted concern that some activities, skills and tasks contained in the home-based developmental activity programme were similar to those tested on the BSID-III. The therapist also expressed concern that the stimulation items and toys were similar to the testing items used in the BSID-III. In order to address this concern, it was deemed important to explain the rationale behind the choice of activities and toys under the rationale and development of the programme, supported by the relevant literature (See 7.3.3). The use of similar items can therefore be justified in that the programme aimed to align the home programme with the assessment findings to provide continuity and to make the test more acceptable to parents (Bedford et al., 2013). Furthermore, the developmental skills contained in the BSID-III are not unique, but represent universal childhood developmental skills across key developmental domains (Bedford et al., 2013).

Based on the panel's suggestions a few additions were made to the programme regarding the development of motor skills:

- Alternatives were to be provided for prone positioning flat on the floor. This included modified prone positioning over angled cushions or on the mothers chest when she was is reclined in a chair or lying down (Hanson, 2015).
- The age at the emergence of hand preference was noted under fine motor skills. Dominance starts to emerge from the age of two to three years of age, but however will be unreliable until the age of five or six years (Scharoun and Bryden, 2014).

Based on the panel's suggestions a few additions were made to the programme regarding the development of motor development skills:

- In the 7-9 month age category: child understands tone of voice was added.
- In the 10-12 month category: child is able to wave bye-bye, shakes head for no and uses sound combinations to refer to an object or person for example "wawa" for a dog was added.

Both speech therapists were of the opinion that more feeding information could be included in the programme. Although feeding is considered an extremely important aspect to address in children with CHD, in light of the frequent occurrence of feeding difficulties and growth failure, care had to be taken not to "overburden" the activity programme and keep it true to its intended purpose. The main aim of the home programme was to promote physical activity and encourage the acquisition of age-appropriate developmental skills within the main domains of development including cognition, socialisation, language and motor skills. From this point of departure it was deemed inappropriate to add any additional information on feeding. In addition, addressing feeding concerns would require the expert assessment and input of a qualified speech therapist.

As the aim of the home programme was also to improve physical endurance and activity tolerance in children with CHD, the researcher deemed it critical to develop guidelines for programme dosage regarding frequency, intensity time (duration) and type of activities

based on the available literature recommendations, as outlined under the rationale and development of the programme (See 7.3.1).

7.7 Presentation of the parent information document

The parent information document is presented in Appendix XX.

7.8. Presentation of the home-based parent-driven developmental activity programme

The home-based, parent-driven developmental activity programme is presented in Appendix XXI. The home programme has also been included in the booklet to provide a tangible experience of the booklet as it will be issued to parents going forward.

7.9 Suggested model for implementation of the homed-based parent-driven developmental activity programme

The final home-based developmental activity programme is ready for piloting and implementation. Based on the clinical experience of the researcher in this population the only viable time for implementation would be on admission for cardiac intervention and prior to discharge.

A proposed model for the implementation of the home-based parent-driven developmental activity programme's implementation for young children with CHD in central SA has been compiled (Refer to Appendix XXII).

CHAPTER 8

CONCLUSION

Over recent decades medical and surgical advances have significantly lowered the mortality rate for children born with congenital heart defects. CHD survivors are at high-risk of growth retardation and developmental morbidity that negatively affect their health-related quality of life (HRQOL). In addition, caring for a child with a chronic health condition such as CHD places a considerable financial and emotional burden on parents, putting them at risk of ongoing stress and psychosocial morbidity including anxiety and depression. The outcomes of children living with CHD and their families in South Africa (SA) are unknown.

The aim of this study was to determine the pre-cardiac intervention and three-month and six-month post-cardiac intervention development, growth, HRQOL and burden of care outcomes of young children with CHD in central SA. Levels of parenting stress served as a proxy for burden of care. Additional objectives included comparing growth, development, HRQOL and parenting stress outcomes over time. The association between numerous variables and developmental, HRQOL and parenting stress outcomes determined. In addition, the developmental needs of young children living with CHD in central SA were to be identified, and a home-based developmental activity programme developed to meet these needs.

In order to meet the Phase I and II objectives, an observational descriptive study was conducted. Forty-eight children aged 30 months and younger and their parents, who met the inclusion criteria, were recruited into the study prior to cardiac intervention at the Universitas Academic Hospital Paediatric Cardiac Unit in Bloemfontein. Development was established by means of the BSID-III, HRQOL by means of the PedsQL^{TM}, and parenting stress by means of the PSI-SF. Growth outcomes were determined by calculating z-scores

for growth parameters using the WHO child growth standards and DS-specific growth charts. Sociodemographic information including maternal age, parental educational attainment and occupational status was collected using a self-developed questionnaire. Medical severity of the child's cardiac disease was rated using the Cardiologists Perception of Medical Severity Scale. Socioeconomic status was determined using the Hollingshead Index of Social Position.

Baseline data was collected for 40 children and their parents. Two children and their parents were excluded following baseline as the children failed to undergo cardiac surgery. In addition, loss to follow-up resulted in data only being collected for 25 parents at three-month and 22 parents at six-month post-cardiac intervention. The attrition rate was high with 47.5% of the children and their families missing at least one follow-up visit.

The majority (75%) of the children in the current study were of black African ethnicity. The median age of the children at baseline was 7.4 months (with a range of 1.4 to 20.9 months). The majority of children (n=26) underwent open-heart surgery in infancy with cardiopulmonary bypass. Most children (n=30) had moderate disease severity, with 20% (n=8) having cyanotic lesions. A quarter of the children (n=10) were also diagnosed with DS. The median age of the mothers at baseline was 30 years (with a range of 16 to 43 years) and the average level of education for both mothers and fathers was grade nine to 11. Most mothers (n=33) did not work outside the home, and the majority of families (n=35) were from a low socioeconomic class. In most instances (97.5%) mothers fulfilled the role of primary caregiver.

The majority (68%) of children had suboptimal growth prior to cardiac intervention. There was significant catch-up growth for both weight (p=0.04) and head circumference (p= 0.02) by the six-month post-cardiac intervention. Complete catch-up growth had not yet taken place by the six-month post-cardiac intervention, with 40.9% of the children still presenting with malnutrition. It is also most likely that small head circumference prior to cardiac-intervention was growth related. The growth trends of children with CHD with DS were found to be similar to those of children with CHD without DS. Growth in children with cyanotic heart defects tended to be poorer both before and after cardiac intervention, but were comparable by six-month post cardiac intervention.

There was a high prevalence of mild to moderate developmental delay across all development domains. Over the study 29% of the children presented with delayed development. On average over the study period 12% of children presented with a delay in at least one area of development, whilst 17% presented with delays in two or more areas of development. Motor delays (27.5%) were most prevalent in younger children, prior cardiac intervention. Motor performance improved with age and post-cardiac intervention, but language and cognitive performance declined with age and increasing skill complexity. There was not a significant change in the developmental outcome of the children over time. The developmental outcome for children with cyanotic and acyanotic heart defects tended to be similar. The presence of DS was the variable found to be most significantly ($p< 0.001$) associated with the developmental outcome of the children across all developmental domains, and at all time points of assessment. Children with CHD with DS tended to have considerably poorer developmental outcomes compared to children with CHD without DS. Disease severity ($p=0.02$) and maternal age ($p=0.01$) were significantly associated with cognitive development. Age at first cardiac surgery was found to be significantly associated with language development both before cardiac intervention ($p <0.01$) and at three-months post-cardiac intervention ($p=0.04$). Suboptimal growth prior to cardiac intervention ($p=0.04$) and maternal age ($p < 0.001$) were significantly associated with motor development.

Although the patterns of development, and the prevalence of developmental delays, in the current studies were similar to those reported in developed countries, children living with CHD in central SA performed below the expected developmental levels for children with CHD when assessed on the BSID-III. Hypotonia was the most significant abnormal neurologic finding, with 45% of the children presenting with hypotonia prior to cardiac intervention. The hypotonia resolved in all children without DS by the six-month post-cardiac intervention.

Overall parents perceived their children's HRQOL as being relatively good, and similar to that of their healthy same-aged peers and other children with CHD in developed countries. Parents' perception of their children's HRQOL improved significantly after cardiac intervention ($p= 0.04$). Perceived HRQOL tended to be similar for children with cyanotic and acyanotic heart defects. Parents of children with CHD with DS tended to perceive their children's HRQOL as poorer than that of children with CHD without DS. Motor development

(p=0.01) and levels of parenting stress (p=0.02) were significantly associated with parental perception of their children's HRQOL prior to cardiac intervention.

The majority of parents' (60%) experienced clinically significant levels of stress prior to their children undergoing cardiac intervention. Parenting stress decreased significantly from pre-cardiac intervention levels at both at three-months (p<0.001) and six-months (p<0.001) post-cardiac intervention as the child's cardiac symptoms resolved or declined, and their health status improved. Parents of children with cyanotic and acyanotic heart defects tended to experience similar levels of stress. Parents of children with CHD with DS tended to experience higher levels of ongoing stress compared with parents of children with CHD without DS. Parenting stress prior to cardiac intervention was significantly associated with parents' perception of their child's HRQOL (p=0.02) and language development (p=0.04). Parenting stress at three-month post-cardiac intervention was significantly associated with age at first cardiac surgery (p=0.03), language development (p=0.03) and level of maternal education (p=0.04). HRQOL and parenting stress outcomes were closely linked before cardiac intervention. Parents who perceived their child as having a poor ability to function in everyday situations showed increased levels of stress.

Based on developmental performance on the BSID-III (subscale scores below 85), 59% of the children in this study would qualify for referral to EI; with many children requiring access to more than one service. A home-based parent-driven developmental activity programme would likely be best suited to meet the developmental needs of children with CHD living in central SA taking into account the need for services, the high rates of loss to follow-up, the long distances to be travelled to the cardiac centres to access services, and the service delivery challenges faced within the public health sector in SA.

Phase III resulted in the development of a home-based developmental activity programme to meet the identified developmental needs of children with CHD in central SA. Qualitative methods, including an expert panel of rehabilitation professionals and a focus group of parents, were used to gain consensus on the content of the developmental activity programme.

It was encouraging that the longer-term outcomes of children with CHD in central SA were not vastly different from those of children in developed countries. The greater extent of the growth retardation and developmental delay of children in the current study is however of concern, and likely attributable to social disadvantage. The findings in this study strongly support the implementation of a CNP as part of standard cardiac care in SA. Moving past the goalpost of survival, and attending to the promotion of optimal outcomes in at-risk children with CHD and their families, it is of critical importance that larger studies with long term follow-up be conducted to identify ways in which to best assist these children and their families. A home-based parent-driven developmental stimulation programme presents an innovative approach to meeting the developmental needs of young children living with CHD in a financial and human resource-constrained environment, challenged by geography.

REFERENCES

Abdel Raheem MM and Mohamed WA. 2012. Impact of congenital heart disease on brain development in newborn infants. *Annals of Paediatric Cardiology* 5(1): 21-26. DOI: 10.4103/0974-2069/93705.

Abdin, R. 1995. Parenting Stress Index Short Form. In *Parenting Stress Index Professional Manual.* Third Edition pp 53-62.

Acton BV, Biggs WSG, Creighton DE, Penner KAH, Switzer HN, Petrie Thomas JH, Joffe AR and Robertson CMT. 2011. Overestimating neurodevelopment using the Bayley-III after early complex cardiac surgery. *Paediatrics* 128: e794-e800.
DOI: 10.1542/peds.2011-0331.

Al-Asy HM, Donia AA, El-Amrosy DM, Rabee E and Bendary AA. 2014. The levels of Ghrelin in children with cyanotic and acyanotic congenital heart disease. *Journal of Paediatric Sciences* 6: e209.
DOI: 10.17334/jps.46761.

Albers CA and Grieve AJ. 2007. Test Review. Bayley N (2006). Bayley Scales of Infant and Toddler Development. Third Edition. San Antonio, TX: Harcourt Assessment. *Journal of Psychoeducational Assessment* 25(2): 180-198.
DOI: 10.1177/0734282906297199.

Albers EL, Bichell DP and McLaughlin B. 2010. New approaches to neuroprotection in infant heart surgery. *Paediatric Research* 68(1): 1-9.
DOI: 10.1203/PDR.0b013e3181df5402.

Alper E, O'Malley TA and Greenwald J. 2016. Hospital discharge and admissions. Auerbach AD (Ed.). In *Up to Date.*
(http://www.uptodate.com/contents/hospital-discharge-and-readmission)
Retrieved on 03 August 2016.

Alsaied T, Marino BS, Esbensen AJ, Anixt JS, Epstein JN and Cnota JF. 2016. Does congenital heart disease affect neurodevelopmental outcomes in children with Down syndrome? *Congenital Heart Disease* 11(1): 26-33.
DOI: 10.1111/chd.12322.

Amakali K and Small LF. 2013. The Plight of parents/ caregivers of children with heart disease in the rural areas of Namibia: A problem of coping. *Global Journal of Health Sciences* 5(2): 62-73.
DOI: 10.5539/gjhs.v5n2p62.

Amedro P, Dorka R, Moniotte S, Guillaumont S, Fraisse A, Kreitmann B, Borm B, Bertet H, Barrea C, Ovaert C, Sluysmans T, De la Villeon G, Vincenti M, Voisin M, Auquier P and Picot MC. 2015. Quality of life of children with congenital heart diseases: A multicentre controlled cross-sectional study. *Paediatric Cardiology*
36: 1588–1601.
DOI 10.1007/s00246-015-1201-x.

American Academy of Paediatrics (AAP). 2006. Active healthy living: Prevention of childhood obesity through increased physical activity. Policy statement by the Council on Sports Medicine and Fitness and Council on School Health. *Paediatrics*
117: 1834- 1842.
DOI: 10.1542/peds.2006-0472.

American Heart Association (AHA). 2015. About congenital heart defects. (http://www.heart.org/HEARTORG/Conditions/CongenitalHeartDefects/Congenital-Heart-Defects_UCM_001090_SubHomePage.jsp#)
Retrieved on 04 December 2015.

Anderson LM, Shinn C, Fullilove MT, Scrimshaw SC, Fielding JE, Normand J, Carande-Kulis VG and the Task Force on Community Preventive Services. 2003. The effectiveness of early childhood development programmes: A systematic review. *American Journal of Preventive Medicine* 24(Suppl 3): 32–46.
DOI: 10.1016/S0749-3797(02)00655-4.

Anderson PJ, de Luca CR, Hutchinson, E, Roberts G, Doyle LW and the Victorian Infant Collaborative Group. 2010. Underestimation of developmental delay by new Bayley III Scale. *Archives of Paediatrics and Adolescent Medicine* 164(4): 352- 356.
DOI: 10.1001/archpediatrics.2010.20.

Angulo-Barroso RM, Schapiro L, Liang W, Rodrigues O, Shafir T, Kaciroti N, Jacobson SW, and Lozoff B. 2011. Motor Development in 9-Month-Old Infants in Relation to Cultural Differences and Iron Status. *Developmental Psychobiology* 53(2): 196–210. DOI: 10:1002/dev.20512.
(http://onlinelibrary.wiley.com/doi/10.1002/dev.20512/epdf)
Retrieved on 25 August 2017.

Ataguba JE, Akazili J and McIntyre D. 2011. Socioeconomic-related health inequality in South Africa: Evidence from General Household Surveys. *International Journal for Equity in Health* 10:48.
DOI: 10.1186/1475-9276-10-48.
(http://www.equityhealthj.com/content/10/1/48)
Retrieved on 19 July 2016.

Aubert EJ. 2015. Motor development in normal children. In Tecklin JS (Ed.). *Paediatric Physical Therapy*. Fifth Edition. Baltimore: Lippincott, Williams and Wilkins p 20.

Baillieu N and Potterton J. 2008. The extent of delay of language, motor and cognitive development in HIV-positive infants. *Journal of Neurologic Physical Therapy*
32: 118–121.
DOI: 10.1097/NPT.0b013e3181846232.

Baker E. 2008. Heart disease from all perspectives. *Cardiology in the Young*
18(2): 123.
DOI: 10.1017/S1047951108002011.

Ballot DE, Potterton J, Chirwa T, Hilburn N and Cooper PA. 2012. Developmental outcome of very low birth weight infants in a developing country. *BMC Paediatrics* 12:11.
DOI: 10.1186/1471-2431-12-11.
(http://www.biomedcentral.com/1471-2431/12/11)
Retrieved on 01 May 2016.

Balter M. 2015. Poverty may affect the growth of children's brains. *Science.* Posted in Brain and Behaviour.
DOI: 10.1126/science.aab0395.
(http://www.sciencemag.org/news/2015/03/poverty-may-affect-growth-children-s-brains)
Retrieved: 28 April 2016.

Bamford L. 2013. Maternal, newborn and child health. In Padarath A and English R (Eds). *South African Health Review 2012/2013*. Durban: Health Systems Trust.
(http://www.hst.org.za/publications/south-african-health-review-2012/13)
Retrieved on 16 February 2016.

Bayley, N. 2006a. Bayley Scales of Infant and Toddler Development Third Edition. Administration Manual. NCS Pearson Inc.

Bayley, N. 2006b. Bayley Scales of Infant and Toddler Development Third Edition. Technical Manual. NCS Pearson Inc.

Beca J, Gunn JK, Coleman L, Hope A, Reed PW, Hunt RW, Finucane K, Brizard C, Dance B and Shekerdemian LS. 2013. New white matter brain injury after infant heart surgery is associated with diagnostic group and the use of circulatory arrest. *Circulation* 127: 971-979.
DOI: 10.1161/CIRCULATIONAHA.112.001089.

Bedford H, Walton S and Ahn J. 2013. Measures of Child Development: A review. Centre for Paediatric Epidemiology and Biostatistics University of Central London Institute of Child Health, London.
(https://www.ucl.ac.uk/cpru/documents/review_of_measures_of_child_development)
Retrieved on 01 September 2016.

Bellinger DC, Jonas RA, Rappaport LA, Wypij D, Wernovsky G, Kuban KCK, Barnes PD, Holmes GI, Hickey PR, Strand RD, Walsh AZ, Helmers SI, Constantinou JE, Carrazana EJ, Mayer JE, Hanley FI, Castaneda AR, Ware JH and Newburger JW. 1995. Developmental and neurologic status of children after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. *The New England Journal of Medicine* 332(9): 549-555. DOI: 10.1056/NEJM199503023320901.

Bellinger DC, Wypij D, Kuban KCK, Rappaport LA, Hickey PR, Wernovsky G, Jonas RA and Newburger JW. 1999. Developmental and neurological status of children at 4 years of age after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. *Circulation*.100: 526-532.
DOI: 10.1161/01.CIR.100.5.526.

Bellinger DC, Wypij D, Du Plessis AJ, Rappaport LA, Jonas RA, Wernovsky G and Newburger JW. 2003. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: The Boston Circulatory Arrest Trial. *The Journal of Thoracic and Cardiovascular Surgery* 126(5): 1385-1396.
DOI: 10.1016/S0022-5223(03)00711-6.

Bellinger DC, Newburger JW, Wypij D, Kuban KCK, du Plesssis AJ and Rappaport LA. 2009. Behaviour at eight years in children with surgically corrected transposition: The Boston Circulatory Arrest Trial. *Cardiology in the Young* 19: 86-97.
DOI: 10.1017/S1047951108003454.

Bellinger DC, Wypij D, Rivkin MJ, DeMaso Robertson RL, Dunbar-Masterson C, Rappaport LA, Wernovsky G, Jonas RA and Newburger JW. 2011. Adolescents with d-transposition of the great arteries corrected with the arterial switch procedure: neuropsychological assessment and structural brain imaging. *Circulation*
124: 1361-1369.
DOI: 10.1161/CIRCULATIONAHA.111.026963.

Benzies KM, Magill-Evans JE, Hayden KA, Ballantyne M. 2013. Key components of early intervention programmes for preterm infants and their parents: A systematic review and meta-analysis. *BMC Pregnancy and Childbirth* 13(Suppl1): S10.
DOI: 10.1186/1471-2393-13-S1-S10.

Berkes A, Varni JW, Pataki I, Kardos L, Kemény C and Mogyorósy G. 2010. Measuring health-related quality of life in Hungarian children attending a cardiology clinic with the Paediatric Quality of Life Inventory™. *European Journal of Paediatrics* 169: 333–347.
DOI: 10.1007/s00431-009-1059-0.

Bernier P-L, Stefanescu A, Samoukovic G and Tchervenkov CI. 2010. The challenge of congenital heart disease worldwide: Epidemiologic and demographic facts. *Seminars in Thoracic and Cardiovascular Surgery: Paediatric Cardiac Surgery Annual* 13: 26-34.
DOI: 10.1053/j.pcsu.2010.02.005.

Bertoletti J, Marx GC, Hattge SP and Pellanda LP. 2015. Health-related quality of life in adolescents with congenital heart disease. *Cardiology in the Young* 25: 526–532.
DOI: 10.1017/S1047951114000304.

Bertoti DB and Schreiner MB. 2015. Intellectual Disabilities: Focus on Down syndrome. In Tecklin JS (Ed.). *Paediatric Physical Therapy*. Fifth Edition. Baltimore: Lippincott, Williams and Wilkins pp 391-396.

Bevilacqua F, Ravà L, Valfrè L, Braguglia A, Zaccara A, Gentile S, Bagolan P and Aite L. 2015. Factors affecting short-term neurodevelopmental outcome in children operated for major congenital anomalies. *Journal of Paediatric Surgery*
50(7): 1125-1129.
DOI: 10.1016/j.jpedsurg.2014.12.015.

Binagwaho A, Rusingiza EK, Mucumbitsi J, Wagner CM, Swain JD, Kagame A, Bukhman G, Uwaliraye P, Nyemazi JP, Nutt CT, Bolman RM, Goldberg H, Lee R, Sluysmans T and de Dieu Ngirabega J. 2013. Uniting to address paediatric heart disease in Africa: Advocacy from Rwanda. *SA Heart* 10(2): 106-107.

Birks Y, Sloper P, Lewin R and Parsons J. 2006. Exploring health-related experiences of children and young people with congenital heart disease. *Health Expectations* 10: 16–29. DOI: 10.1111/j.1369-7625.2006.00412.x.

Bjarnason-Wehrens B, Dordel S, Schickendantz S, Krumm C, Bott D, Sreeram N and Brockmeier K. 2007a. Motor development in children with congenital cardiac diseases compared to their healthy peers. *Cardiology in the Young* 17(5): 487-98. DOI: 10.1017/S1047951107001023.

Bjarnason-Wehrens B, Dordel S, Sreeram N and Brockmeier K. 2007b. Cardiac rehabilitation in congenital heart disease. In Perk J, Mathes P, Gohlke H, Monpère C, Hellemans I, McGee H, Sellier P and Saner H (Eds). *Cardiovascular Prevention and Rehabilitation.* London: Springer-Verlag pp 364-375.

Blauw-Hospers CH, de Graaf-Peters VB, Dirk T, Bos AF and Hadders-Algra M. 2007. Does early intervention in infants at high risk for a developmental motor disorder improve motor and cognitive development? *Neuroscience & Biobehavioural Reviews* 31(8): 1201-1212. DOI: 10.1016/j.neubiorev.2007.04.010.

Blauw-hospers CH, Dirks T, Hulshof LJ, Bos AF and Hadders-Algra M. 2011. Paediatric physical therapy in infancy: From nightmare to dream? A two-arm randomised trial. *Physical Therapy* 91(9): 1323-38. DOI: 10.2522/ptj.20100205.

Blössner M and de Onis M. 2005. Malnutrition: Quantifying the health impact at national and local levels. Geneva, World Health Organisation, 2005. (WHO Environmental Burden of Disease Series, No. 12). (http://www.who.int/nutgrowthdb/publications/quantifying_health_impact/en/) Retrieved on 20 May 2016.

Bogart LM, Skinner D, Thurston IB, Toefy Y, Klein DJ, Hu CH, and Schuster MA. 2013. *Lets Talk!* A South African worksite-based HIV prevention parenting programme. *Journal of Adolescent Health* 53(5): 602-608.
DOI: 10.1016/j.jadohealth.2013.01.014.

Bonnier C. 2008. Evaluation of early stimulation programs for enhancing brain development. *Acta Paediatrica* 97: 853–858.
DOI: 10.1111/j.1651-2227.2008.00834.x.

Bos AF. 2013. Bayley-II or Bayley-III: What do the scores tell us? *Developmental Medicine & Child Neurology* 55: 978–979.
DOI: 10.1111/dmcn.12234.

Boston Children's Hospital. 2016. Cardiac neurodevelopmental programme: Overview. (http://www.childrenshospital.org/centers-and-services/cardiac-neurodevelopmental-program)
Retrieved on 01 October 2016.

Bradshaw D, Groenewald P, Laubscher R, Nannan N, Nojilana B, Norman R, Pieterse D, Schneider M, Bourne DE, Timaeus IM, Dorrington R and Johnson L. 2003. Initial burden of disease estimates for South Africa, 2000. *South African Medical Journal* 93(9): 682-688.

Bravo-Valenzuela NJM, Passarelli MLB, Coates MV and Nascimento LFC. 2011. Weight and height recovery in children with Down syndrome and congenital heart disease. *Brazilian Journal of Cardiovascular Surgery* 26(1): 61-68.

Brosig CL, Mussatto KA, Kuhn EM and Tweddell JS. 2007. Psychosocial outcomes for preschool children and families after surgery for complex congenital heart disease. *Paediatric Cardiology* 28: 255–262.
DOI: 10.1007/s00246-006-0013-4.

Brosig Soto C, Olude O, Hoffmann RG, Bear L, Chin A, Dasgupta M and Mussatto K. 2011. Implementation of a routine developmental follow-up programme for children with congenital heart disease: Early results. *Congenital Heart Disease*
6(5): 451–460.
DOI: 10.1111/j.1747-0803.2011.00546.x.

Brosig C, Butcher J, Butler S, Ilardi DL, Sananes R, Sanz JH, Sood E, Struemph K and Ware J. 2014. Monitoring developmental risk and promoting success for children with congenital heart disease: Recommendations for cardiac neurodevelopmental follow-up programmes. *Clinical Practice in Paediatric Psychology* 2 (2): 153-165.
DOI: 10.1037/cpp0000058.

Brown SC. 2014. Screening for congenital heart disease. (Paper presented at the 5th Child Health Priorities Conference in Bloemfontein, South Africa from 3 to 5 December 2014). University of the Free State, Bloemfontein.

Brown SC. 2016. Outcome of severe forms of CHD in South Africa. (Unpublished personal correspondence). University of the Free State, Bloemfontein.

Bruce E, Lilja C and Sundin K. 2014. Mothers' lived experiences of support when living with young children with congenital heart defects. *Journal for Specialists in Paediatric Nursing* 19*:* 54–67.
DOI: 10.1111/jspn.12049.

Car J, Gurol-Urganci I, de Jongh T, Vodopivec-Jamsek V and Atun R. 2012. Mobile phone messaging reminders for attendance at healthcare appointments. *Cochrane Database of Systematic Reviews* (7): 1-38.
DOI: 10.1002/14651858.CD007458.pub2.

Carey LK, Nicholson BC and Fox RA. 2002. Maternal factors related to parenting young children with congenital heart disease. *Journal of Paediatric Nursing*
17(3): 174-183.
DOI: 10.1053/jpdn.2002.124111.

Carte Blanche. 2016. Mechanical hearts.
(https://carteblanche.dstv.com/mechanical-hearts/)
Retrieved on 25 August 2017.

Cassedy A, Drotar D, Ittenbach R, Hottinger S, Wray J, Wernovsky G, Newburger JW, Mahony L, Mussatto K, Cohen MI and Marino BS. 2013. The impact of socioeconomic status on health-related quality of life for children and adolescents with heart disease. *Health and Quality of Life Outcomes* 11: 99.
DOI: 10.1186/1477-7525-11-99.
(http://www.hqlo.com/content/11/1/99)
Retrieved on 17 May 2016.

Centre for Disease Control and Prevention (CDC). 2006. Gaining consensus amongst stakeholders through the nominal group technique. Evaluation Brief number 7.
(http://www.cdc.gov/healthyyouth/evaluation/pdf/brief7.pdf)
Retrieved 30 August 2013.

Centre for Disease Control and Prevention (CDC). 2015. Facts about congenital heart disease: Data and statistics.
(http://www.cdc.gov/ncbddd/heartdefects/facts.html)
Retrieved on 08 December 2015.

Centre for Disease Control and Prevention (CDC). 2016a. Health-related quality of life.
(http://www.cdc.gov/hrqol/concept.htm)
Retrieved on 27 May 2016.

Centre for Disease Control (CDC). 2016b. Growth charts for children with Down syndrome.
(http://www.cdc.gov/ncbddd/birthdefects/downsyndrome/growth-charts.html)
Retrieved on: 02 July 2016.

Chaix MA, Andelfinger G and Khairy P. 2016 Genetic testing in congenital heart disease: A clinical approach. *World Journal of Cardiology* 8(2): 180-191.
DOI: 10.4330/wjc.v8.i2.180.

Charleton PM, Dennis J and Marder E. 2010. Medical management of children with Down syndrome. *Paediatrics and Child Health* 20(7): 331-337.
DOI: 10.1016/j.paed.2010.06.006.

Chock VY, Chang IJ, and Reddy VM. 2012. Short-term neurodevelopmental outcomes in neonates with congenital heart disease: The era of newer surgical strategies. *Congenital Heart Disease* 7: 544–550.
DOI: 10.1111/j.1747-0803.2012.00678.x.

Colditz P, Sanders MR, Boyd R, Pritchard M, Gray P, O'Callaghan MJ, Slaughter V, Whittingham K, O'Rourke P, Winter L, Evans T, Herd M, Ahern J and Jardine L. 2015. Prem Baby Triple P: A randomised controlled trial of enhanced parenting capacity to improve developmental outcomes in preterm infants. *BMC Paediatrics* 15:15.
DOI: 10.1186/s12887-015-0331-x.

Cole SZ and Lanham JS. 2011. Failure to Thrive: An update. *American Family Physician* 83(7): 829-834.
(http://www.aafp.org/afp/2011/0401/p829.pdf)
Retrieved on 20 May 2016.

Columbia University Leaders Project. 2013. Test review: Bayley Scales of Infant and Toddler Development: Third edition. Columbia University, New York.
(http://www.leadersproject.org/2013/11/25/test-review-bayley-iii/)
Retrieved on 05 March 2016.

Conger RD, Conger KJ, and MJ Martin. 2010. Socioeconomic status, family processes, and individual development. *Journal of Marriage and Family*
72(3): 685-704.
DOI: 10.1111/j.1741-3737.2010.00725.x.

Connor JA, Kline NE, Mott S, Harris SK and Jenkins KJ. 2010. The meaning of cost for families of children with congenital heart disease. *Journal of Paediatric Health Care* 25(4): 318-325.
DOI: 10.1016/j.pedhc.2009.09.002.

Cooper PJ, Tomlinson M, Swartz L, Landman M, Molteno C, Stein A, McPherson K and Murray L. 2009. Improving quality of mother-infant relationship and infant attachment in socioeconomically deprived community in South Africa: randomised controlled trial. *British Medical Journal* 338: b974.
DOI: 10.1136/bmj.b974.

Costello CL, Gellatly M, Daniel J, Justo RN and Weir C. 2015. Growth restriction in infants and young children with congenital heart disease. *Congenital Heart Disea*se 10(5): 447–456.
DOI: 10.1111/chd.12231.

Cuskelly M, Hauser-Cram P and VanRiper M. 2008. Families of children with Down syndrome: What we know and what we need to know. *Down syndrome Research and Practice* pp 105-113.
DOI: 10.3104/reviews.2079.
(https://www.down-syndrome.org/reviews/2079/)
Retrieved on 08 May 2016.

Da Rosa Pereira K, Firpo C, Gasparin M, Teixeira AR, Dornelles S, Bacaltchuk T and Levy DA. 2015. Evaluation of swallowing in infants with congenital heart defect. *International Archives of Otorhinolaryngology* 19: 55–60.
DOI: 10.1055/s-0034-1384687.

Davidson J, Gringras P, Fairhurst C and Simpson J. 2015. Physical and neurodevelopmental outcomes in children with single-ventricle circulation. *Archives of Disease in Childhood* 100: 449–453.
DOI: 10.1136/archdischild-2014-306449.

Daymont C, Neal A, Prosnitz A, and Cohen MS. 2013. Growth in children with congenital heart disease. *Paediatrics* 131(1): e236 –e242.
DOI: 10.1542/peds.2012-1157.

DeMaso DR, Campis LK, Wypij D, Bertram S, Lipshitz M and Freed M. 1991.
The impact of maternal perceptions and medical severity on the adjustment of children with congenital heart disease. *Journal of Paediatric Psychology* 16(2): 137-149.

Deshpande SR, Maher KO and Morales DL. 2016. Mechanical circulatory support in children: Challenges and opportunities. *Progress in Paediatric Cardiology 43: 31-41.*
DOI: 10.1016/j.ppedcard.2016.08.016
(http://ac.els-cdn.com/S1058981316300741/1-s2.0-S1058981316300741-main.pdf?_tid=3b045218-8b14-11e7-b21c-00000aacb35d&acdnat=1503830646_f55bb15c8d59b17f91b3527508a88a94)
Retrieved on 25 August 2017.

Dittrich H, Bührer C, Grimmer, Dittrich S, Abdul-Khaliq H and Lange PE. 2003. Neurodevelopment at 1 year of age in infants with congenital heart disease. *Heart* 89(4): 436-441.
DOI:10.1136/heart.89.4.436.

Dobush G. 2015. How mobile phones are changing the developing world.
(https://www.cta.tech/News/Blog/Articles/2015/July/How-Mobile-Phones-Are-Changing-the-Developing-Worl.aspx)
Retrieved on: 02 August 2016.

Doherty N, McCusker CG, Molloy B, Mulholland C, Rooney N, Craig B, Sands A, Stewart M and Casey F. 2009. Predictors of psychological functioning in mothers and fathers of infants born with severe congenital heart disease. *Journal of Reproductive and Infant Psychology* 27(4): 390–400.
DOI: 10.1080/02646830903190920.

Domi T, Edgell DS, McCrindle BW, Williams WG, Chan AK, MacGregor DL, Kirton A and de Veber GA. 2008. Frequency, predictors, and neurologic outcomes of vaso-occlusive strokes associated with cardiac surgery in children. *Paediatrics*
122:1292- 1298.
DOI: 10.1542/peds.2007-1459.

Donofrio MT and Massaro AN. 2010. Impact of congenital heart disease on brain development and neurodevelopmental outcome. *International Journal of Paediatrics* Volume 2010: Article ID 359390.
DOI: 10.1155/2010/359390.

Donofrio MT, du Plessis AJ and Limperopoulos C. 2011. Impact of congenital heart disease on foetal brain development and injury. *Current Opinion in Paediatrics*
23: 502–511.
DOI:10.1097/MOP.0b013e32834aa583.

Downer A, Meara J, Costa A and Sethuraman K. 2006. SMS text messaging improves outpatient attendance. *Australian Health Review* 30(3): 389-396.
(http://www.publish.csiro.au/?act=view_file&file_id=AH060389.pdf)
Retrieved on 25 March 2016.

Du Q, Zhou X, Wang X, Chen S, Yang X, Chen N, Liang J, Deng W and Sun K. 2015. Passive movement and active exercise for very young infants with congenital heart disease: a study prottext medsscol for a randomized controlled trial. *Trials* 16: 288.
DOI: 10.1186/s13063-015-0816-9.

Dudek-Shriber L and Zelazny S. 2007.The Effects of Prone Positioning on the Quality and Acquisition of Developmental Milestones in Four-Month-Old Infants. Paediatric Physical Therapy 19:48 –55.
DOI: 10.1097/01.pep.0000234963.72945.b1

Dulfer K, Duppen N, Van Dijk APJ, Kuipers IM, Van Domburg RT, Verhulst FC, Van der Ende J, Helbing WA and Utens EMWJ. 2015. Parental mental health moderates the efficacy of exercise training on health-related quality of life in adolescents with Congenital Heart Disease. *Paediatric Cardiology* 36: 33–40.
DOI: 10.1007/s00246-014-0961-z.

Eagleson KJ, Justo RN, Ware RS, Johnson SG and Boyle FM. 2013. Health-related quality of life and congenital heart disease in Australia. *Journal of Paediatrics and Child Health* 49: 856–864.
DOI: 10.1111/jpc.12296.

Edmeston M and Francis K. 2014. Beyond band-aids: Reflections on public and private health care in South Africa. Helen Suzman Foundation publications.
(http://hsf.org.za/resource-centre/focus/focus-67/MEdmeston_KFrancis.pdf/view)
Retrieved on 27 March 2016.

Edwin F, Tettey M, Aniteye E, Tamatey M, Sereboe L, Entsua-Mensah K, Kotei D and Baffoe-Gyan K. 2011. The development of cardiac surgery in West Africa - The case of Ghana. *Pan African Medical Journal* 9:15.
DOI: 10.11604/pamj.2011.9.15.848.

Elmagrpy Z, Rayani A, Shah A, Habas E and Aburawi EH. 2011. Down syndrome and congenital heart disease: Why the regional difference as observed in the Libyan experience? *Cardiovascular Journal of Africa* 22(6): 306- 309.
DOI: 10.5830/CVJA-2010-072.

ENCA News Channel. 2015. Unemployment rate rises to 26.4% says Stats SA, media release, 15May 2015, ENCA
(https://www.enca.com/money/unemployment-rate-rises-264-q1-2015)
Viewed 20 July 2016.

Engle PL, Black MM, Behrman JR, Cabral de Mello M, Gertler PJ, Kapiriri L, Martorell R, Eming Young M and the International Child Development Steering Group. 2007. Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. *The Lancet* 369: 229–242.
DOI: 10.1016/S0140-6736(07)60112-3.

Fonseca A, Nazaré, B and Canavarro MC. 2012. Parental psychological distress and quality of life after a prenatal or postnatal diagnosis of congenital anomaly: A controlled comparison study with parents of healthy infants. *Disability and Health Journal* 5: 67-74.
DOI: 10.1016/j.dhjo.2011.11.001.

Franck LS, Mcquillan A, Wray J, Grocott MPW and Goldman A. 2010. Parent stress levels during children's hospital recovery after congenital heart surgery. *Paediatric Cardiology* 31: 961–968.
DOI 10.1007/s00246-010-9726-5.

Fulbright Sumpter S. 2009. The relationships between parenting stress, growth, and development in infants with congenital heart defects during the first six months of life. (Unpublished PhD thesis). University of Pennsylvania, Philadelphia.
(http://repository.upenn.edu/cgi/viewcontent.cgi?article=1090&context=edissertations)
Retrieved 08 August 2016.

Fuller S, Nord AS, Gerdes M, Wernovsky G, Jarvik GP, Bernbaum J, Zackai E and Gaynor JW. 2009. Predictors of impaired neurodevelopmental outcomes at one year of age after infant cardiac surgery. *European Journal of Cardiothoracic Surgery*
36: 40-48.
DOI: 10.1016/j.ejcts.2009.02.047.

Fung A, Manlhiot C, Naik S, Rosenberg H, Smythe J, Lougheed J, Mondal T, Chitayat D, McCrindle BW and Mital S. 2013. Impact of prenatal risk factors on congenital heart disease in the current era. *Journal of the American Heart Association*
2(3): e000064.
DOI: 10.1161/JAHA.113.000064.

Garcia Guerra G, Joffe AR, Robertson CMT, Atallah J, Alton G, Sauve RS, Dinu IA, Ross DB, Rebeyka IM and the Western Canadian Complex Paediatric Therapies Follow-up Group. 2014. Health-related quality of life experienced by children with chromosomal abnormalities and Congenital Heart Defects. *Paediatric Cardiology*
35: 536–541.
DOI: 10.1007/s00246-013-0820-3.

Gaynor JW, Seung Kim D, Arrington CB, Atz AM, Bellinger DC, Burt AA, Ghanayem NS, Jacobs JP, Lee TM, Lewis AB, Mahle WT, Marino BS, Miller SG, Newburger JW, Pizarro C, Ravishankar C, Santani AB, Wilder NS, Jarvik GP, Mital S and Russell MW. 2014. Validation of association of the Apolipoprotein E ε2 allele with neurodevelopmental dysfunction after cardiac surgery in neonates and infants. *Journal of Thoracic and Cardiovascular Surgery* 148(6): 2560-2566.
DOI: 10.1016/j.jtcvs.2014.07.052.

Gaynor JW, Stopp C, Wypij D, Andropoulos DB, Atallah J, Atz AM, Beca J, Donofrio MT, Duncan K, Ghanayem NS, Goldberg CS, Hövels-Gürich H, Ichida F, MDI, Jacobs JP, Justo R, Latal B, Li JS, Mahle WT, McQuillen PS, Menon SC, Pemberton VL, Pike NA, Pizarro C, Shekerdemian LS, Synnes A, Williams I, Bellinger DC and Newburger JW for the International Cardiac Collaborative on Neurodevelopment (ICCON) investigators. 2015. Neurodevelopmental outcomes after cardiac surgery in infancy. *Paediatrics* 135(5): 816-825.
DOI: 10.1542/peds.2014-3825.

Gazit AZ, Gandhi SK and Canter CC. 2010. Mechanical Circulatory Support of the Critically Ill Child Awaiting Heart Transplantation. *Current Cardiology Reviews* 6 (1): 46-53.
DOI: 10.2174/157340310790231617
(file:///C:/Users/SmithRobyn/Downloads/CCR-6-46.pdf)
Retrieved on 25 August 2017

Gerber AU, Hompanera Torre A, Büscher G, Stock SAK, Graf C, Schickendantz S, Brockmeier K and Lüngen M. 2010. Direct non-medical and indirect costs for families with children with congenital cardiac defects in Germany: A survey from a university centre. *Cardiology in the Young* 20: 178-185.
DOI: 10.1017/S1047951109991995.

Gerdes M and Flynn T. 2010. Clinical assessment of neurobehavioral outcomes in infants and children with congenital heart disease. *Progress in Paediatric Cardiology* 29: 97–105.
DOI: 10.1016/j.ppedcard.2010.06.009.

Gersh B. 2011. Prevention of heart disease and healthcare delivery in South Africa: Challenges and opportunities. *SA Heart* 8(2): 90-95.

Gessler P, Schmitt B, Prétre R and Latal B. 2009. Inflammatory response and neurodevelopmental outcome after open-heart surgery in children. *Paediatric Cardiology* 30: 301–305.
DOI 10.1007/s00246-008-9354-5.

Girgis A, Lambert S, Johnson C, Waller A and Currow D. 2013. Physical, psychosocial, relationship, and economic burden of caring for people with cancer: A review. *Journal of Oncology Practice* 9(4): 197-202.
DOI: 10.1200/JOP.2012.000690.

Gocha-Marchese V. 2015. Paediatric Oncology. In Tecklin JS (Ed.). *Paediatric Physical Therapy*. Fifth edition. Philadelphia: Lippincott Williams and Wilkins
pp 598-600.

Goff DA, Luan X, Gerdes M, Bernbaum J, D'Agostino JA, Rychik J, Wernovsky G, Licht DJ, Nicolson SC, Clancy RC, Spray TL and Gaynor JW. 2011. Younger gestational age is associated with worse neurodevelopmental outcomes after cardiac surgery in infancy. *Journal of Thoracic and Cardiovascular Surgery* 143(3): 535-542.
DOI: 10.1016/j.jtcvs.2011.11.029.

Goldbeck L and Melches J. 2005. Quality of life in families of children with congenital heart disease. *Quality of Life Research* 14:1915–1924.
DOI: 10.1007/s11136-005-4327-0.

Goldberg S, Morris P, Simmons RJ, Fowler RS, and Levison H. 1990. Chronic illness in infancy and parenting stress: A comparison of three groups of parents. *Journal of Paediatric Psychology* 15(3): 347-358.
DOI: 10.1093/jpepsy/15.3.347.

Goldberg CS, Mussatto K, Licht D and Wernovsky G. 2011. Neurodevelopment and quality of life for children with hypoplastic left heart syndrome: Current knowns and unknowns. *Cardiology in the Young* 21(Suppl. 2): 88–92.
DOI: 10.1017/S104795111100165X.

Goldberg L. 2011. An evaluation of the health-related quality of life of children with HIV/AIDS. (Unpublished MSc in Physiotherapy). University of the Witwatersrand, Johannesburg.

Golfenshtein N, Srulovici E and Medoff-Cooper B. 2016. Investigating parenting stress across paediatric health conditions - A systematic review. *Comprehensive Child and Adolescent Nursing* 39(1): 41-79.
DOI: 10.3109/01460862.2015.1078423.

GOOGLE images. 2016. Map of the provinces of South Africa.
(http://www.towns.bookingsouthafrica.com)
Retrieved on 01 September 2016.

Gould C and Ward CL. 2015. Positive parenting in South Africa. Why supporting families is key to development and violence prevention. Institute for Security Studies, Policy Brief 77.
(https://www.issafrica.org/uploads/PolBrief77.pdf)
Retrieved on 20 July 2016.

Grantham-McGregor SM, Fernald LC and Sethuraman K. 1999. Effects of health and nutrition on cognitive and behavioural development in children in the first three years of life. Part 1: Low birth weight, breastfeeding, and protein- energy malnutrition. *Food and Nutrition Bulletin* 20(1): 53-75.

Grantham-McGregor S, Bun Cheung Y, Cueto S, Glewwe P, Richter L, Strupp B and the International Child Development Steering Group 2007. Developmental potential in the first 5 years for children in developing countries. *The Lancet* 369: 60–70.
DOI: 10.1016/S0140-6736(07)60032-4.

Grønning Dale MT, Solberg Ø, Holmstrøm H, Landolt MA, Eskedal LT and Vollrath ME. 2013. Well-being in mothers of children with congenital heart defects: a 3-year follow-up. *Quality of Life Research* 22: 2063–2072.
DOI: 10.1007/s11136-012-0326-0.

Gruber PJ and Epstein JA. 2004. Development Gone Awry: Congenital Heart Disease. *Circulation Research* 94: 273-283.
DOI: 10.1161/01.RES.000011644.43797.3B.

Gunn JK, Beca J, Hunt RW, Olischar M and Shekerdemian LK. 2012. Perioperative amplitude-integrated EEG and neurodevelopment in infants with congenital heart disease. *Intensive Care Medicine* 38: 1539-1547.
DOI 10.1007/s00134-012-2608-y.

Gupta N, Castillo-Laborde C and Landry MD. 2011. Health-related rehabilitation services: Assessing the global supply of and need for human resources. *BMC Health Services Research* 11: 276.
(http://www.biomedcentral.com/1472-6963/11/276)
Retrieved: 09 August 20016.

Hanson, H. 2015. Cardiac disorders. In Tecklin JS (Ed.). *Paediatric Physical Therapy.* Fifth Edition. Philadelphia: Lippincott Williams and Wilkins pp 657- 663; 671-675.

Hartman DM and Medoff-Cooper B. 2012. Transition to home after neonatal surgery for congenital heart sisease. *The American Journal of Maternal/Child Nursing* 37(2): 95-100.
DOI:10.1097/NMC.0b013e318241dac1.

Harvey KA, Kovalesky A, Woods RK, and Loan LA. 2013. Experiences of mothers of infants with congenital heart disease before, during, and after complex cardiac surgery. *Heart & Lung* 42: 399-406.
DOI: 10.1016/j.hrtlng.2013.08.009.

Haskell WL, Lee I-M, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD and Bauman A. 2007. Physical Activity and Public Health: Updated Recommendation for Adults From the American College of Sports Medicine and the American Heart Association. *Circulation* 116:1081-1093.
DOI: 10.1161/CIRCULATIONAHA.107.185649.

Haskett ME, Ahern LS, Ward CS and Allaire JC. 2006. Factor Structure and Validity of the Parenting Stress Index–Short Form**.** *Journal of Clinical Child and Adolescent* 35(2): 302–312.
DOI: 10.1207/s15374424jccp3502_14.

Hearps SJ, McCarthy MC, Muscara F, Hearps SJC, Burke K, Jones B and Anderson VA. 2014. Psychosocial risk in families of infants undergoing surgery for a serious congenital heart disease. *Cardiology in the Young* 24: 632–639.
DOI: 10.1017/S1047951113000760.

Hoffman JIE and Kaplan S. 2002. The Incidence of congenital heart disease. *Journal of the American College of Cardiology* 39(12): 1890-1900.
DOI: 10.1016/S0735-1097(02)01886-7

Hoffman JIE. 2013. The global burden of congenital heart disease. *Cardiovascular Journal of Africa* 24(4): 141-145.
DOI: 10.5830/CVJA-2013-028.

Hollingshead AB. 1975. Four factor index of social status. (Unpublished paper). Yale University, New Haven.

Homsy J, Zaidi S, Shen Y, Ware JS, Samocha KE, Karczewski KJ, de Palma SR , McKean D, Wakimoto H, Gorham, Jin SC, Deanfield J, Giardini A, Porter GA Jr., Kim R, Bilguvar K, López-Giráldez F, Tikhonova I, Mane S, Romano-Adesman A, Qi H, Vardarajan B, Ma L, Daly M, Roberts AE, Russell MW, Mital S, Newburger JW, Gaynor JW, Breitbart RE, Iossifov I, Ronemus M, Sanders SJ, Kaltman JR, Seidman JG, Brueckner M, Gelb BD, Goldmuntz E, Lifton RP, Seidman CE and Chung WK. 2015. *De novo* mutations in congenital heart disease with neurodevelopmental and other congenital anomalies. *Science* 350(6265): 1262-1266.
DOI: 10.1126/science.aac9396.

Hoosen EGM, Cilliers AM, Hugo-Hamman CT, Brown SC, Harrisberg JR, Takawira FF, Govendregaloo K, Lawrenson J and Hewitson, J. 2010a. Audit of paediatric cardiac services in South Africa. *SA Heart* 7(1): 4-9.

Hoosen EGM, Cilliers AM, Hugo-Hamman CT, Brown SC, Harrisberg JR, Takawira FF, Govendregaloo K, Lawrenson J and Hewitson J. 2010b. Optimal paediatric cardiac services in South Africa – What do we need? A Statement of the Paediatric Cardiac Society of South Africa. *SA Heart* 7(1): 10-16.

Hoosen EGM, Cilliers AM, Hugo-Hamman CT, Brown SC, Lawrenson JB, Zühlke L. and Hewitson J. 2011. Paediatric cardiac services in South Africa. *South African Medical Journal* 101(2): 106-107.

Hoskoppel A, Roberts H, Kugler J, Duncan K and Needleman H. 2010. Neurodevelopmental outcomes in infants after surgery for congenital heart disease: A comparison of single ventricle versus two-ventricle physiology. *Congenital Heart Disease* 5: 90-95.
DOI: 10.1111/j.1747-0803.2009.00373.x.

Hövels-Gürich HH, Konrad K, Skorzenski D, Nacken C, Minkenberg R, Messmer BJ and Seghaye M-C. 2006. Long-term neurodevelopmental outcome and exercise capacity after corrective surgery for tetralogy of Fallot or ventricular septal defect in infancy. *The Annals of Thoracic Surgery* 81: 958-966.
DOI: 10.1016/j.athoracsur.2005.09.010.

Hövels-Gürich HH, Konrad K, Skorzenski D, Minkenberg R, Herpertz-Dahlmann B, Messmer BJ and Seghaye MC. 2007. Long-term behaviour and quality of life after corrective cardiac surgery in infancy for tetralogy of Fallot or ventricular septal defect. *Paediatric Cardiology* 28: 346–354.
DOI: 10.1007/s00246-006-0123-z.

Howell BA and Tapley C. 2012. Thoracic Surgery. In Cambell SK, Palisano RJ and Orlin MN (Eds). *Physical Therapy for Children*. Fourth Edition. St. Louis: Elsevier Saunders pp 845-846; 857-868.

Hutchings J and Potterton J. 2014. Developmental delay in HIV-exposed infants in Harare, Zimbabwe. *Vulnerable Children and Youth Studies* 9(1): 43–55.
DOI: 10.1080/17450128.2013.778440.

Irving SY. 2011. Patterns of weight change in infants with congenital heart disease following neonatal surgery: potential predictors of growth failure. (Unpublished PhD thesis). University of Pennsylvania, Pennsylvania.
(http://repository.upenn.edu/edissertations/443)
Retrieved on 26 April 2016.

Jary S, Whitelaw A, Walløe L and Thoresen M. 2013. Comparison of Bayley-2 and Bayley-3 scores at 18 months in term infants following neonatal encephalopathy and therapeutic hypothermia. *Developmental Medicine & Child Neurology*
55: 1053–1059.
DOI: 10.1111/dmcn.12208.

Jenkins K, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, Elixson M, Warnes CA and Webb CL. 2007. Non-inherited risk factors and congenital cardiovascular defects: Current knowledge. A Scientific Statement from the American Heart Association Council on cardiovascular disease in the young. *Circulation*
115: 2995-3014.
DOI: 10.1161/CIRCULATIONAHA.106.183216.

Johnson S, Moore T and Marlow N. 2014. Using the Bayley-III to assess neurodevelopmental delay: Which cut-off should be used? *Paediatric Research* 75(5): 670 -674.
DOI: 10.1038/pr.2014.10.

Jones J and Hunter D. 1995. Consensus methods for medical and health services research. *British Medical Journal* 311: 1376-1380.

Joynt CA, Robertson CMT, Cheung P-Y, Nettel-Aguirre A, Joffe AR, Sauve RS, Biggs WSG, Leonard NJ, Ross DB, Rebeyka IM and the Western Canadian Complex Paediatric Therapies Follow-up Group. Two-year neurodevelopmental outcomes of infants undergoing neonatal cardiac surgery for interrupted aortic arch: A descriptive analysis. 2009. *The Journal of Thoracic and Cardiovascular Surgery* 138: 924-932.
DOI: 10.1016/j.jtcvs.2009.03.016.

Kader M and Perera NK. 2014. Socioeconomic and nutritional determinants of low birth weight in India. *North American Journal of Medical Sciences* 6(7): 302–308.
DOI: 10.4103/1947-2714.136902.

Kemper AR, Mahle WT, Martin GR, Cooley WC, Kumar P, Morrow WR, Kelm K, Pearson GD, Glidewell J, Grosse SD and Howell RR. 2011. Strategies for implementing screening for critical congenital heart disease. *Paediatrics*
128: e1295-e1267.
DOI: 10.1542/peds.2011-1317.

Kendall L, Sloper P, Lewin JP and Parsons JM. 2003. Views of parents concerning the planning for rehabilitation of families of children with CHD. *Cardiology in the Young* 13: 20-27.
DOI: 10.1017/S1047951103000052.

Kengne AP and Mayosi BM. 2013. A snapshot of cardiovascular disease in Africa in the new millennium. *Cardiovascular Journal of Africa* 24(4): 104-105.

Kinsley RH, Edwin F, Colsen PR, Mamorare H, Martin G and Brink J. 2011. Paediatric cardiac surgery for a continent – The experience of the Walter Sisulu Paediatric Cardiac Centre for Africa. *SA Heart* 8(2): 122-129.

Kinsley RH. 2012. The Third Aldo Castañeda Lecture: The Neglect of Neonatal/Infant Cardiac Disease in Africa − Continental Genocide? *World Journal for Paediatric and Congenital Heart Surgery* 3: 241-243.
DOI: 10.1177/2150135111425394.

Kitzinger J. 1995. Introducing focus groups. *British Medical Journal* 311: 299-302.

Knirsch W, Zingg W, Bernet V, Balmer C, Dimitropoulos A, Prêtre R, Bauersfeld U and Latal B. 2010. Determinants of body weight gain and association with neurodevelopmental outcome in infants operated for congenital heart disease. *Interactive Cardiovascular and Thoracic Surgery* 10: 377-382.
DOI: 10.1510/icvts.2009.216135.

Knowles RL and Bull C. 2012. Longer-term survival and health outcomes for children living with congenital heart defects. *Paediatrics and Child Health* 23(2): 74-77.
DOI: 10.1016/j.paed.2012.09.005.

Knowles RL, Day T, Wade A, Bull C, Wren C and Dezateux C, on behalf of the UK Collaborative Study of Congenital Heart Defects. 2014. Patient-reported quality of life outcomes for children with serious congenital heart defects. *Archives of Disease in Childhood* 99: 413–419.
DOI: 10.1136/archdischild-2013-305130.

Knutson S, Kelleman MS and Kochilas L. 2016. Implementation of Developmental Screening Guidelines for Children with Congenital Heart Disease. *Journal of Paediatrics* 176:135-41
DOI: 10.1016/j.jpeds.2016.05.029

Kucik JE, Nembhard WN, Donohue P, Devine O, Wang Y, Minkovitz CS and Burke T. 2014. Community socioeconomic disadvantage and the survival of infants with congenital heart defects. *American Journal of Public Health* 104:150–157.
DOI: 10.2105/AJPH.2014.302099.

Laing S, McMahon C, Ungerer J, Taylor A, Badawi N and Spence K. 2010. Mother–child interaction and child developmental capacities in toddlers with major birth defects requiring newborn surgery. *Early Human Development* 86: 793–800.
DOI: 10.1016/j.earlhumdev.2010.08.025.

Lakshman M, Charles M, Biswas M, Sinha L and Arora NK. 2000. Focus group discussions in medical research. *Indian Journal of Paediatrics* 67(5): 358-62.

Lan S-F, Mu, P-F and Hsieh K-S. 2007. Maternal experiences making a decision about heart surgery for their young children with congenital heart disease. *Journal of Clinical Nursing* 16(12): 2323-2330.
DOI: 10.1111/j.1365-2702.2007.02004.x.

Landolt MA, Valsangiacomo Buechel ER and Latal B. 2008. Health-related quality of life in children and adolescents after open-heart surgery. *The Journal of Paediatrics* 152: 349-55.
DOI: 10.1016/j.jpeds.2007.07.010.

Landolt MA, Valsangiacomo Buechel E and Latal B. 2011. Predictors of parental quality of life after child open heart surgery: A 6-month prospective study. *The Journal of Paediatrics* 158: 37-43.
DOI: 10.1016/j.jpeds.2010.06.037.

Lantos, GP. 2015. *Consumer behaviour in action. Real life applications for marketing managers*. New York: Routlege pp 226 -227.
Lata K, Mishra D, Mehta V and Juneja M. 2015. Neurodevelopmental status of children aged 6-30 months with congenital heart disease. *Indian Paediatrics*
52: 957-960.

Latal B, Helfricht S, Fischer JE, Bauersfeld U and Landolt MA. 2009. Psychological adjustment and quality of life in children and adolescents following open-heart surgery for congenital heart disease: A systematic review. *BMC Paediatrics* 9: 6.
DOI: 10.1186/1471-2431-9-6.

Lawoko S and Soares JJF. 2002. Distress and hopelessness among parents of children with congenital heart disease, parents of children with other diseases, and parents of healthy children. *Journal of Psychosomatic Research* 52: 193–208.
DOI: 10.1016/S0022-3999(02)00301-X.

Lawoko S and Soares JJF. 2006. Psychosocial morbidity among parents of children with congenital heart disease: A prospective longitudinal study. *Heart & Lung*
35: 301–314.
DOI: 10.1016/j.hrtlng.2006.01.004.

Lee S, Yoo J-S and Yoo I-Y. 2007. Parenting Stress in mothers of children with congenital heart disease. *Asian Nursing Research* 1(2): 116-124.
DOI: 10.1016/S1976-1317(08)60014-6.

Lee KB. 2014. Paediatric cardiac surgery in developing countries of Africa: Current state and future direction. (Unpublished MD thesis). University of Texas, Dallas.

Leong K., Chen W, Leong K, Mastura I, Mimi O, Sheikh M, Zailinawati A, Ng C, Phua K and Teng C. 2006. The use of text messaging to improve attendance in primary care: A randomised control trial. *Family Practice Advance Access*
23(6): 699-705.
DOI: 10.1093/fampra/cml044.

Lewin RJP, Kendall L and Sloper P. 2002. Provision of services for rehabilitation of children and adolescents with congenital cardiac disease: A survey of centres for paediatric cardiology in the United Kingdom. *Cardiology in the Young* 12: 412–414.

Liamlahi R, Von Rhein M, Bührer S, Valsangiacomo Buechel ER, Knirsch W, Landolt MA and Latal B. 2014. Motor dysfunction and behavioural problems frequently coexist with congenital heart disease in school-age children. *Acta Paediatrica*
103: 752-758.
DOI: 10.1111/apa.12639.

Limperopoulos C, Majnemer A, Shevell MI, Rosenblatt B, Rohlicek C and Tchervenkov C. 2000. Neurodevelopmental status of newborns and infants with congenital heart defects before and after open-heart surgery. *The Journal of Paediatrics* 137(5): 638-645.
DOI: 10.1067/mpd.2000.109152.

Limperopoulos C, Annette Majnemer A, Shevell MI, Charles Rohlicek C, Rosenblatt B, Tchervenkov C and Darwish HZ. 2002. Predictors of developmental disabilities after open heart surgery in young children with congenital heart defects. *The Journal of Paediatrics* 141(1): 51-58.
DOI:10.1067/mpd.2002.125227.

Long SH, Eldridge BJ, Galea MP and Harris SR. 2011. Risk factors for gross motor dysfunction in infants with congenital heart disease. *Infants & Young Children*
24(3): 246-258.
DOI: 10.1097/IYC.0b013e3182176274.

Long SH, Galea MP, Eldridge BJ and Harris SR. 2012a. Performance of 2-year-old children after early surgery for congenital heart disease on the Bayley Scales of Infant and Toddler Development, Third Edition. *Early Human Development* 88: 603–607.
DOI: 10.1016/j.earlhumdev.2012.01.007.

Long SH, Harris SR, Eldridge BJ and Galea MP. 2012b. Gross motor development is delayed following early cardiac surgery. *Cardiology in the Young* 22(5): 574 -582.
DOI: 10.1017/S1047951112000121.

Long SH, Eldridge BJ, Harris SR and Cheung MMH. 2015. Challenges in trying to implement an early intervention programme for infants with congenital heart disease. *Paediatric Physical Therapy* 27: 38-43.
DOI: 10.1097/PEP.0000000000000101.

Lowe JR, Erickson SJ, Schrader R and Duncan AF. 2012. Comparison of the Bayley II Mental Developmental Index and the Bayley III Cognitive Scale: Are we measuring the same thing? *Acta Paediatrica* 101(2): e55–e58.
DOI: 10.1111/j.1651-2227.2011.02517.x.

Lucile Packard Children's Hospital. 2015. 3West Purple Team Guidelines Handbook. Stanford University p 33.
(http://peds.stanford.edu/Rotations/purple_team/pdfs/3W%20Handbook%202015.pdf)
Retrieved on 01 December 2015.

Lunn PG. 2002. Growth retardation and stunting of children in developing countries. *British Journal of Nutrition* 88: 109–110.
DOI: 10.1079/BJN2002652.

Macran S, Birks Y, Parsons J, Sloper P, Hardman G, Kind P, VanDoorn C, Thompson D and Lewin R. 2006. The development of a new measure of quality of life for children with congenital cardiac disease. *Cardiology in the Young* 16: 165–172.
DOI: 10.1017/S1047951106000102.

Madaschi V, Coutinho Macedo E, Pontrelli Mecca T and Silvestre Paula C. 2016. Bayley-III Scales of Infant and Toddler Development: Transcultural adaptation and psychometric properties. *Paidéia* 26(64): 189-197.
DOI: 10.1590/1982-43272664201606.

Mahle, WT. 2015. Developmental testing important part of care for children with congenital heart disease. *American Academy of Paediatrics News* 36(5). Focus on sub-specialities.
(http://www.aappublications.org/content/36/5/12.1)
Retrieved on 05 January 2016.

Majnemer A, Limperopoulos C, Shevell M, Rosenblatt B, Rohlicek C and Tchervenkov C. 2006a. Long-term neuromotor outcome at school entry of infants with congenital heart defects requiring open-heart surgery. *Journal of Paediatrics* 148: 72-7.
DOI: 10.1016/j.jpeds.2005.08.036.

Majnemer A, Limperopoulos C, Shevell M, Rohlicek C, Rosenblatt B and Tchervenkov C. 2006b. Health and well-being of children with congenital cardiac malformations, and their families, following open-heart surgery. *Cardiology in the Young* 16: 157–164.
DOI: 10.1017/S1047951106000096.

Majnemer A, Limperopoulos C, Shevell MI, Rohlicek C, Rosenblatt B, and Tchervenkov C. 2009. A new look at outcomes of infants with congenital heart disease. *Paediatric Neurology* 40(3): 197-204.
DOI: 10.1016/j.pediatrneurol.2008.09.014.

Majnemer A, Limperopoulos C, Shevell M, Rohlicek C, Rosenblatt B and Tchervenkov C. 2012. Gender differences in the developmental outcomes of children with congenital cardiac defects. *Cardiology in the Young* 22: 514-519.
DOI: 10.1017/S1047951111002071.

Marino BS, Tomlinson RS, Drotar D, Claybon ES, Aguirre A, Ittenbach R, Welkom JS, Helfaer MA, Wernovsky G and Shea JA. 2009. Quality-of-Life concerns differ among patients, parents, and medical providers in children and adolescents with congenital and acquired heart disease. *Paediatrics* 123: e708-e715.
DOI: 10.1542/peds.2008-2572.

Marino BS, Uzark K, Ittenbach R and Drotar D. 2010. Evaluation of quality of life in children with heart disease. *Progress in Paediatric Cardiology* 29: 131-138.
DOI: 10.1016/j.ppedcard.2010.06.008.

Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, Mussatto KA, Uzark K, Goldberg CS, Johnson WH, Li J, Smith SE, Bellinger DC and Mahle WT on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Stroke Council. 2012. Neurodevelopmental Outcomes in children with Congenital Heart Disease: Evaluation and management. A Scientific Statement from the American Heart Association. *Circulation* 126: 1143-1172.
DOI: 10.1161/CIR.0b013e318265ee8a.

Marino BS. 2013. New concepts in predicting, evaluating, and managing neurodevelopmental outcomes in children with congenital heart disease. *Current Opinion in Paediatrics* 25: 574-584.
DOI: 10.1097/MOP.0b013e328365342e.

Marino BS, Cassedy A, Drotar D and Wray J. 2016. The impact of neurodevelopmental and psychosocial outcomes on health-related quality of life in survivors of congenital heart disease. *Journal of Paediatrics* 174:11-22.e2.
DOI: 10.1016/j.jpeds.2016.03.071.

Mars M. 2011. Telerehabilitation in South Africa – Is there a way forward?
International Journal of Telerehabilitation 3(1): 11-18.
DOI: 10.5195/ijt.2011.6069.

Martinez-Biarge M, Jowett VC, Cowan FM and Wusthoff CJ. 2013. Neurodevelopmental outcome in children with congenital heart disease. *Seminars in Foetal & Neonatal Medicine* 18: 279-285.
DOI: org/10.1016/j.siny.2013.04.006.

Martorell, R. 1999. The nature of child malnutrition and its long-term implications. (http://fnb.sagepub.com/content/20/3/288.full.pdf)
Retrieved on 15 May 2016.

Matsuzaki T, Matsui M, Ichida F, Nakazawa J, Hattori A, Yoshikosi K, Miyazaki M, Fujii M, Hagino I, Kagisaki K and Yagihara T. 2010. Neurodevelopment in 1-year-old Japanese infants after congenital heart surgery. *Paediatrics International*
52: 420–427.
DOI: 10.1111/j.1442-200X.2009.02974.x.

Mbewu A. 2009. The burden of cardiovascular disease in sub-Saharan Africa. *SA Heart* 6(1): 4-10.

McConnell D, Parakkal M, Savage A and Rempel G. 2014. Parent-mediated intervention: Adherence and adverse effects. *Disability and Rehabilitation*
37(10): 864-72.
DOI: 10.3109/09638288.2014.946157.

McCrindle BW, Clarizia NA, Khaikin S, Holtby HM, Manlhiot C, Schwartz SM, Caldarone CA, Coles JG, VanArsdell GS, Scherer SW and Redington AN. 2014. Remote ischaemic preconditioning in children undergoing cardiac surgery with cardiopulmonary bypass: A single-canter double-blinded randomised trial. *Journal of the American Heart Association* 3: e000964.
DOI: 10.1161/JAHA.114.000964.

McCusker CG, Doherty NN, Molloy B, Rooney N, Mulholland C, Sands A, Craig B, Stewart M and Casey F. 2009. A controlled trial of early interventions to promote maternal adjustment and development in infants born with severe congenital heart disease. *Child Care, Health and Development* 36(1): 110–117.
DOI: 10.1111/j.1365-2214.2009.01026.x.

McCusker CG, Armstrong MP, Mullen M, Doherty NN and Casey FA. 2013.
A sibling-controlled, prospective study of outcomes at home and school in children with severe congenital heart disease. *Cardiology in the Young* 23: 507–516.
DOI: 10.1017/S1047951112001667.

McGowan JE, Alderdice FA, Holmes VA and Johnston L. 2011. Early childhood development of late-preterm infants: A systematic review. *Paediatrics*
127(6): 1111-1124.
DOI: 10.1542/peds.2010-2257.

McKelvey LM, Whiteside-Mansell L, Faldowski RA, Shears J, Ayoub C and Hart AD. 2009. Validity of the short form of the Parenting Stress Index for fathers of toddlers. *Journal of Child and Family Studies* 18(1): 102-111.
DOI: 10.1007/s10826-008-9211-4.

Medoff-Cooper B, Irving SY, Hanlon AL, Golfenshtein N. Radcliffe J, Stallings VA, Marino BS and Ravishankar C. 2016. The association among feeding mode, growth and developmental outcomes in infants with complex CHD at 6 and 12 months of age. *Journal of Paediatrics* 159: 154-159.
DOI: org/10.1016/j.jpeds.2015.10.017.

Mellion K, Uzark K, Cassedy A, Drotar D, Wernovsky G, Newburger JW, Mahony L, Mussatto K, Cohen M, Limbers C, and Marino BS for the Pediatric Cardiac Quality of Life Inventory Testing Study Consortium. 2014. Health-related quality of life outcomes in children and adolescents with congenital heart disease. *The Journal of Paediatrics* 164: 781-788.
DOI: org/10.1016/j.jpeds.2013.11.066.

Menahem S, Poulakis Z and Priorc M. 2008. Children subjected to cardiac surgery for congenital heart disease. Part 2 – Parental emotional experiences. *Interactive Cardiovascular and Thoracic Surgery* 7: 605–608.
DOI: 10.1510/icvts.2007.171066.

Miatton M, de Wolf D, Francois K, Thiery E and Vingerhoets G. 2007. Behaviour and self-perception in children with a surgically corrected congenital heart disease. *Journal of Developmental & Behavioural Paediatrics 28:* 294–301.
DOI: 10.1097/DBP.0b013e3180cabc3c

Miles AC. 2007. Substance use, parenting stress and child maltreatment: Exploring these relationships in a sample of at-risk mothers. (Unpublished M. in Clinical Psychology). University of Cape Town, Cape Town.

Mocumbi AO, Lameira E, Yaksh A, Paul L, Ferreira MB and Sidi D. 2011. Challenges on the management of congenital heart disease in developing countries. *International Journal of Cardiology* 148: 285–288.
DOI: 10.1016/j.ijcard.2009.11.006.

Mohammed S, Kaurs E, Aguirre VP, Varni JW and Alonso EM. 2016. Health-related quality of life in infants with chronic liver disease. *Journal of Paediatric Gastroenterology and Nutrition* 62(5): 751-756.
DOI: 10.1097/MPG.0000000000001054.

Moola FJ. 2012. “This is the best fatal illness that you can have”: Contrasting and comparing the experiences of parenting youth with cystic fibrosis and congenital heart disease. *Quality of Life Research* 22(2): 212–225.
DOI: 10.1177/1049732311421486.

Moore T, Johnson S, Haider S, Hennessy E and Marlow N. 2012. Relationship between test scores using the second and third editions of the Bayley Scales in extremely preterm children. The *Journal of Paediatrics* 160: 553-558.
DOI: 10.1016/j.jpeds.2011.09.047.

Mörelius E, Lundh U and Nelson N. 2002. Parenting stress in relation to the severity of congenital heart disease in offspring. *Paediatric Nursing* 28(1): 28-34.

Morrow B. 2012. Chest physiotherapy in the paediatric cardiac intensive care unit. (Lecture presented as part of the Cardiopulmonary Physiotherapy 1 course in Bloemfontein 2012). University of Cape Town, Cape Town.

Mughal AR, Sadiq M, Hyder SN, Qureshi AU, Shah SSA, Khan MA and Nasir JA. 2011. Socioeconomic status and impact of treatment on families of children with congenital heart disease. *Journal of the College of Physicians and Surgeons Pakistan* 21(7): 398-402.
DOI: 07.2011/JCPSP.398402.

Müller J, Pringsheim M, Engelhardt A, Meixner J, Halle M, Oberhoffer R, Hess J and Hager A. 2013. Motor training of sixty minutes once per week improves motor ability in children with congenital heart disease and retarded motor development: A pilot study. *Cardiology in the Young* 23: 717-721.
DOI: 10.1017/S1047951112001941.

Murphy AM, Neill CA and Zuckerberg AL. 2006. Syndromes and congenital heart defects. In Nichols DG, Ungerleider RM, Spevak PJ, Greeley WJ, Cameron DE, Lappe DG and Wetzel RC (Eds). *Critical Heart Disease in Infants and Children*. Second Edition. Philadelphia: Mosby Elsevier pp 952-954.

Mussatto K. 2006. Adaptation of the child and family to life with a chronic illness. *Cardiology in the Young* 16(Suppl.3): 110–116.
DOI: 10.1017/S104795110600103X.

Mussatto K and Tweddell J. 2005. Quality of life following surgery for congenital cardiac malformations in neonates and infants. *Cardiology in the Young*
15(Suppl1): 174–178.

Mussato KA. 2006. Beyond survival: What are the outcomes that really matter to our patients? *Cardiology in the Young* 16: 125–127.
DOI: 10.1017/S1047951106000035

Mussatto KA, Hoffmann RG, Hoffman GM, Tweddell JS, Bear L, Cao Y and Brosig C. 2014. Risk and prevalence of developmental delay in young children with Congenital Heart Disease. *Paediatrics* 133:1–8.
DOI: 10.1542/peds.2013-2309.

Mussatto KA, Hoffmann R, Hoffman G, Tweddell JS, Bear L, Cao Y, Tanem J, and Brosig C. 2015. Risk factors for abnormal developmental trajectories in young children with congenital heart disease. *Circulation* 132: 755-761.
DOI: 10.1161/CIRCULATIONAHA.114.014521.

Myrelid A Gustafsson J, Ollars, B and Anneren G. 2002. Growth charts for Down's syndrome from birth to 18 years of age. *Archives of Disease in Childhood*
87: 97–103.

Naguib AN, Winch PD, Tobias JD, Yeates KO, Miao Y and Galantowicz M. 2015. Neurodevelopmental outcome after cardiac surgery utilising cardiopulmonary bypass in children. *Saudi Journal of Anaesthesia* 9(1): 12-18.
DOI: 10.4103/1658-354X.146255.

National Human Research Ethics Council of South Africa (NHREC). 2012. Payment of trial participants in South Africa: Ethical considerations for research ethics committees. (http://research.ukzn.ac.za/Files/National%20Guidelines%20for%20Payment%20of%20Participants%20in%20Clinical%20Trials%20(2012).pdf)
Retrieved on 20 February 2013.

Nolte E and McKee M. 2008. Caring for people with chronic conditions: An introduction. In Nolte E and McKee (Eds). *Caring for people with chronic conditions. A health system perspective*. New York: McGraw-Hill Education p1.

Nousi, D and Christou, A. 2010. Factors affecting quality of life in children with congenital heart disease. *Health Sciences Journal* 4(2): 94-100.

Novak I and Cusick A. 2006. Home programmes in paediatric occupational therapy for children with cerebral palsy: Where to start? *Australian Occupational Therapy Journal* 53: 251–264.
DOI: 10.1111/j.1440-1630.2006.00577.x.

Novak I, Cusick A and Lowe K. 2007. A pilot study on the impact of occupational therapy home programming for young children with Cerebral Palsy. *American Journal of Occupational Therapy* 61: 463–468.

Novak I, Cusick A and Lannin N. 2009. Occupational therapy home programmes for cerebral palsy: Double blind, randomised, controlled trial. *Paediatrics* 124: e606–e614.
DOI: 10.1542/peds.2009-0288.

Novak I. 2011. Parent experience of implementing effective home programmes. *Physical & Occupational Therapy in Paediatrics* 31(2): 198–213.
DOI: 10.3109/01942638.2010.533746.

Okoromah CAN, Ekure EN, Lesi FEA, Okunowo WO, Tijani BO and Okeiyi JC. 2011. Prevalence, profile and predictors of malnutrition in children with congenital heart defects: A case–control observational study. *Archives of Disease in Childhood*
96: 354–360.
DOI: 10.1136/adc.2009.176644.

Owen M, Shevell M, Majnemer A and Limperopoulos C. 2011. Abnormal brain structure and function in newborns with complex congenital heart defects before open-heart surgery: A review of the evidence. *Journal of Child Neurology*
26: 743-755.
DOI: 10.1177/0883073811402073.

Paediatric Congenital Heart Association (PCHA). 2014. Educational resources. (http://conqueringchd.org)
Retrieved on 05 December 2015.

Palisano RJ, Cambell SK and Harris, S. 2012. Evidence based decision making. In Cambell SK, Palisano RJ and Orlin MN (Eds). *Physical Therapy for Children*. Fourth Edition. St. Louis: Elsevier Saunders pp110-113.

Patel SS and Burns TL. 2013. Non-genetic risk factors and congenital heart defects. *Paediatric Cardiology* 34(7): 1535-55.
DOI: 10.1007/s00246-013-0775-4.

Paradis J. 2005. Grammatical morphology in children learning English as a second language: Implications of similarities with specific language impairment. *Language, Speech, and Hearing Services in Schools* 36: 172–187.
DOI: 10.1044/0161-1461(2005/019).

PAREXEL International. 2010. Informed consent. (Unpublished course manual). Parexel International Research Regulatory Compliance presented Good Clinical Practice Course presented in Bloemfontein on 02 November 2010.

Pelchat D, Ricard N, Bouchardy J-M, Perreault M, SaucierJ-F, Berthiaumey M and Bisson J. 1999. Adaptation of parents in relation to their 6-month-old infant's type of disability. *Child: Care, Health and Development* 25(4): 377-397.

Pēna ED and Quinn R. 1997. Task Familiarity. Effects on the test performance of Puerto Rican and African American Children. *Language, Speech, and Hearing Services in Schools* 28: 323-332.
DOI: 10.1044/0161-1461.2804.323.

Penn A. 2013. The effect of childhood brain tumours on the child and family: A prospective multidisciplinary follow up of. (Unpublished PhD thesis). University of Witwatersrand, Johannesburg.

Pérez-Padilla J, Menéndez S and Lozano O. 2015. Validity of the Parenting Stress Index Short Form in a sample of at-risk mothers. *Evaluation Review* 39(4): 428-46.
DOI: 10.1177/0193841X15600859.
Pew Research Centre. 2015. Cell Phones in Africa: Communication Lifeline.
(http://www.pewglobal.org/2015/04/15/cell-phones-in-africa-communication-lifeline/)
Retrieved on 02 August 2016.

Pike NA, Evangelista LS, Doering LV, Koniak-Griffin D, Lewis AB and Child JS. 2007. Health-related quality of life: A closer look at related research in patients who have undergone the Fontan operation over the last decade. *Heart & Lung* 36(1): 3-15.
DOI: 10.1016/j.hrtlng.2006.06.002.

Potterton J, Stewart A and Cooper P. 2007. Parenting stress of caregivers of young children who are HIV Positive. *African Journal of Psychiatry* 10: 210-214.

Potterton J, Stewart A, Cooper P and Becker P. 2010. The effect of a basic home stimulation programme on the development of young children infected with HIV. *Developmental Medicine & Child Neurology* 52: 547–551.
DOI: 10.1111/j.1469-8749.2009.03534.x.

Pugin A. 2007. The relationship between severity of cerebral palsy in children and the levels of stress experienced by their parents. (Unpublished MSc in Physiotherapy). University of Witwatersrand, Johannesburg.

Raat H, Mohangooa AD and Grootenhuis MA. 2006. Paediatric health-related quality of life questionnaires in clinical trials. *Current Opinion in Allergy and Clinical Immunology* 6: 180–185.
DOI: 10.1097/01.all.0000225157.67897.c2.

Rademeyer V and Jacklin L. 2013. A study to evaluate the performance of black South African urban infants on the Bayley Scales of Infant Development III. *South African Journal of Child Health* 7(2): 54-59.
DOI: 10.7196/SAJCH.547.

Raj M, Paul M, Sudhakar A, Varghese AA, Haridas AC, Kabali C and Kumar RK. 2015. Micro-Economic Impact of Congenital Heart Surgery: Results of a prospective study from a limited-resource setting. *Plos ONE* e1-e13.
DOI: 10.1371/journal.pone.0131348 June 25, 2015 1/13.
(http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0131348)
Retrieved on 25 May 2016.

Rappaport, L. 2015. Neurodevelopmental outcome in children with congenital Heart Disease: A work in progress. *Paediatrics* 135(5): 926-927.
DOI: 10.1542/peds.2015-0719.

Ravishankar C, Zak V, Williams, Bellinger DC, Gaynor JW, Ghanayem NS, Krawczeski CD, Licht DJ, Mahony L, Newburger JW, Pemberton VL, Williams RV, Sananes R, Cook TL, Atz T, Khaikin S and Hsu DT. 2013. Association of impaired linear growth and worse neurodevelopmental outcome in infants with single ventricle physiology: A report from the Paediatric Heart Network Infant Single Ventricle Trial. *Journal of Paediatrics* 162(2): 250–256.
DOI: 10.1016/j.jpeds.2012.07.048.

Reitman D, Currier RO and Stickle TR. 2002. A critical evaluation of the Parenting Stress Index-Short Form (PSI-SF) in a head start population. *Journal of Clinical Child and Adolescent Psychology* 31(3): 384–392.
DOI: 10.1207/S15374424JCCP3103_10.

Rempel GR, Ravindran V, Rogers LG and Magill-Evans J. 2013. Parenting under Pressure: A grounded theory of parenting young children with life-threatening congenital heart disease. *Journal of Advanced Nursing* 69(3): 619–630.
DOI: 10.1111/j.1365-2648.2012.06044.x.

Republic of South Africa - Department of Health (RSA-DoH). 2006. Guideline for good clinical practice in the conduct of clinical trials with human participants in South Africa. Department of Health: Pretoria, South Africa pp 17-18; 69.

Reuters South Africa. 2015. The burden of cardiovascular disease in sub-Saharan Africa. South Africa lacks cardiologists, media release, 21 October 2015, SABC news. (http://www.sabc.co.za/news/a/e59438804a59f1539cfcdf6d39fe9e0c/SouthundefinedAfricaundefinedlacksundefinedcardiologists-20152610)
Viewed on 01 November 2016.

Rhodan M. 2013. Saving U.S. healthcare with Skype. Presented in the healthcare editorial in *TIME* online on 16 September 2013.
(http://swampland.time.com/2013/09/16/saving-u-s-health-care-with-skype/)
Accessed 07 April 2016.

Riehle-Colarusso T, Autry A, Razzaghi H, Boyle, CA, Mahle WT, VanNaarden Braun K and Correa A. 2015. Congenital Heart Defects and Receipt of Special Education Services. *Paediatrics* 136(3): 496-504.
DOI: 10.1542/peds.2015-0259.

Riner WF and Hunt Selhorst H. 2013. Physical activity and exercise in children with chronic health conditions. *Journal of Sport and Health Science* 2(1): 12 -20.
DOI: 10.1016/j.jshs.2012.11.005.

Risley T. R and Hart B. 2006. Promoting early language development. In Watt NF, Ayoub C, Bradley RH, Puma JE and le Boeuf WA (Eds). *The crisis in youth mental health: Critical issues and effective programmes. Volume 4: Early intervention programmes and policies.* Westport CT: Praeger pp 83-88.

Robertson A. 2006. Chronic conditions in children. In Ijumba P and Padarath A (Eds). *South African Health Review 2006*. Durban: Health Systems Trust.
(http://www.hst.org.za/uploads/files/begining_06.pdf)
Retrieved on 15 June 2013.

Robertson CMT, Sauve RS, Joffe AR, Alton GW, Moddemann, DM, Blakley PM, Synnes AR, Dinu IA, Harder JR, Soni R, Bodani JP, Kakadekar AP, Dyck JD, Human DG, Ross DB and Rebeyka IM. 2011. The registry and follow-up of Complex Paediatric Therapies Programme of Western Canada: A mechanism for service, audit, and research after life-saving therapies for young children. *Cardiology Research and Practice* Volume 2011: Article ID 96574.
DOI: 10.4061/2011/965740.

Rollins CK and Newburger JW. 2014. Neurodevelopmental Outcomes in Congenital Heart Disease. *Circulation* 130: e124-e126.
DOI: 10.1161/CIRCULATIONAHA.114.008556.

Roman B. 2011. Nourishing little hearts: Nutritional implications for Congenital Heart Defects. In *Practical Gastroenterology* Parrish CR (Ed.).
Series 8 pp 11-34.
(https://med.virginia.edu/ginutrition/wpcontent/uploads/sites/199/2014/06/RomanArticle.pdf)
Retrieved on 26 April 2016.

Roman VA, Makwakwa T and Lacante M. 2016. Perceptions of parenting styles in South Africa: The effects of gender and ethnicity. *Cogent Psychology* 3: 1153231.
DOI: 10.1080/23311908.2016.1153231.

Rosenberg SA, Robinson CC, Shaw EF and Ellison MC. 2013. Part C early intervention for infants and toddlers: Percentage eligible versus served. *Paediatrics* 131: 38–46.
DOI:10.1542/peds.2012-1662.

Rosmarakis ES, Vergidisa PI, Soteriadesa ES, Paraschakisa K, Papastamatakia PA and Falagasa ME. 2005. Estimates of global production in cardiovascular diseases research. *International Journal of Cardiology* 100: 443–449.
DOI: 10.1016/j.ijcard.2004.11.005.

Russel DC, Kriel H, Joubert G and Goosen Y. 2009. Prone positioning and motor development in the first six weeks of life. *South African Journal of Occupational Therapy* 39(1): 11-14.

Russell DC, Van Heerden R, Van Vuuren S, Venter A and Joubert G. 2016. Time management guidelines for the intervention of a child with Down syndrome using the Developmental "Resource Stimulation Programme" (DRSP). *South African Journal of Occupational Therapy* 46(1): 41-44.
DOI: 10.17159/2310-3833/2016/v46n1a9.

Sadoh WE, Nwaneri DU and Owobu AC. 2011. The cost of outpatient management of chronic heart failure in children with congenital heart disease. *Nigerian Journal of Clinical Pra*ctice 14(1): 65-69.
DOI: 10.4103/1119-3077.79255.

Sagoe D. 2012. Precincts and prospects in the use of focus groups in social and behavioural science research. *The Qualitative Report* 17(29): 1-16.
(http://nsuworks.nova.edu/cgi/viewcontent.cgi?article=1784&context=tqr)
Retrieved on 20 March 2016.

Said-Mohamed R, Micklesfield LK, Pettifor JM and Norris SA. 2015. Has the prevalence of stunting in South African children changed in 40 years? A systematic review. *BMC Public Health* 15:534.
DOI: 10.1186/s12889-015-1844-9.

Sananes R, Manlhiot C, Kelly E, Hornberger LK, Williams WG, MacGregor D, Buncic R and McCrindle BW. 2012. Neurodevelopmental outcomes after open heart operations before 3 months of age. *The Annals of Thoracic Surgery* 93: 1577–83.
DOI: 10.1016/j.athoracsur.2012.02.011.

Sand P, Kljajić M and Sunnegårdh J. 2013. The reliability of the Paediatric Quality of Life Inventory 3.0 Cardiac Module™ for Swedish children with congenital heart defects. *Nordic Psychology* 65(3): 210-223.
DOI: 10.1080/19012276.2013.824204.

Sarajuuri A, Lönnqvist T, Mildh L, Rajantie I, Eronen M, Mattila I and Jokinen E. 2009. Prospective follow-up study of children with univentricular heart: Neurodevelopmental outcome at age 12 month. *Journal of Thoracic and Cardiovascular Surgery* 137(1): 139-145.
DOI: 10.1016/j.jtcvs.2008.06.025.

Sarrechia I, Miatton M, Francois C, Gewillig M, Meyns B, Vingerhoets G and de Wolf DI. 2015. Neurodevelopmental outcome after surgery for acyanotic congenital heart disease. *Research in Developmental Disabilities* 45–46: 58-68.
DOI: org/10.1016/j.ridd.2015.07.004.

Schaefer C, Von Rhein M, Knirsch W, Huber R, Natalucci G, Caflisch J, Landolt MA and Latal B. 2013. Neurodevelopmental outcome, psychological adjustment, and quality of life in adolescents with congenital heart disease. *Developmental Medicine & Child Neurology* 55:1143–1149.
DOI: 10.1111/dmcn.12242.

Scharoun SM and Bryden PJ. 2014. Hand preference, performance abilities, and hand selection in children. *Frontiers in Psychology* 5: 82.
DOI: 10.3389/fpsyg.2014.00082.

Schlensak C. 2005. Myocardial protection in congenital heart surgery. *Multimedia Manual of Cardiothoracic Surgery* pp 1-5.
DOI: 10.1510/mmcts.2004.000729.

Sena Leal L, Morais da Silva RL, Siqueira Coelho Aita KM, de Araújo Monteiro RP, Carvalho de Montalvão T. 2016. Assessment of Motor Development of Children with Congenital Heart Disease. *International Journal of Cardiovascular Sciences*
29(2): 103-109.
DOI: 10.5935/2359-4802.20160017.

Simelane, A. 2015. The role of resilience and socioeconomic status in the parenting of children with autism spectrum disorder. (Unpublished MA in Psychology). University of Witwatersrand, Johannesburg.

Simons JS, Glidden R, Sheslow D and Pizarro C. 2010. Intermediate neurodevelopmental outcome after repair of Ventricular Septal Defect. *Annals of Thoracic Surgery* 90: 1586-92.
DOI: 10.1016/j.athoracsur.2010.06.082.

Smit FE. 2015. Hearts in sight – A pretty picture of collapse and excellence. *SA Heart* 12(4): 194-196.

Snookes SH, Gunn JK, Eldridge BJ, Donath SM, Hunt RW, Galea MP Sherkerdemian L. 2010. A systematic review of motor and cognitive outcomes after early surgery for congenital heart disease. *Paediatrics* 25(4): e818-827.
DOI:10.1542/peds.2009-1959.

Solberg Ø, Grønning Dale MT, Holmstrøm H,Eskedal LT, Landolt MA and Vollrath ME. 2011. Long-Term Symptoms of Depression and Anxiety in Mothers of Infants with Congenital Heart Defects. *Journal of Paediatric Psychology* 36(2): 179–187.
DOI: 10.1093/jpepsy/jsq054.

Soulvie MA, Desai PP, Parker White C and Sullivan BN. 2012. Psychological distress experienced by parents of young children with congenital heart defects: A comprehensive review of literature. *Journal of Social Service Research* 38: 484–502.
DOI: 10.1080/01488376.2012.696410.

Spearing, E. 2015. Providing Family-centred care in paediatric physical therapy. In Tecklin JS (Ed.). *Paediatric Physical Therapy.* Fifth edition. Philadelphia: Lippincott Williams and Wilkins pp 1-2; 10.

Spijkerboer AW, de Koning WB, Duivenvoorden HJ, Bogersd AJJC, Verhulsta FC, Helbing WA and Utens EMWJ. 2010. Medical predictors for long-term behavioural and emotional outcomes in children and adolescents after invasive treatment of congenital heart disease. *Journal of Paediatric Surgery* 45: 2146-2153.
DOI: 10.1016/j.jpedsurg.2010.07.026.

Spittle AJ, Orton J, Doyle LW, Boyd R. 2007. Early developmental intervention programmes post hospital discharge to prevent motor and cognitive impairment in preterm infants. *Cochrane Database Systematic Reviews* 2: CD005495.
DOI: 10.1002/14651858.CD005495.pub3.

Srichantaranit A, Chontawan R, Yenbut J, Ray L, Laohaprasittiporn D and Wanitkun S. 2010. Thai families' caring practices for infants with congenital heart disease prior to cardiac surgery. *Pacific Rim International Journal of Nursing Research* 14(1): 61-78.

Starr, JA and Tucker CA. 2005. The cardiopulmonary system. In Effgen S (Ed.). *Meeting the physical therapy needs of children*. Philadelphia: F. A. Davies Company pp 296-302.

Statistics South Africa. 2012. Census 2011 Statistical release – P0301. Pretoria, South Africa.
(http://www.statssa.gov.za/publications/P03014/P030142011.pdf)
Retrieved on 01 March 2016.

Statistics South Africa. 2013. Gender Statistics in South Africa, 2011.
(http://www.statssa.gov.za/publications/Report-03-10-05/Report-03-10-052011.pdf)
Retrieved on 19 July 2016.

Statistics South Africa. 2014. Mid-year population estimates 2014 statistical release P0302. (https://www.statssa.gov.za/publications/P0302/P03022015.pdf)
Retrieved on 25 April 2016.

Statistics South Africa. 2015. General Household Survey 2014. Statistical Release pp 11; 29.
(http://www.statssa.gov.za/publications/P0318/P03182014.pdf)
Retrieved on 09 August 2016.

Steiber NA, Gilmour S, Morra A, Rainbow J, Robitaille S, VanArsdell G, McCridnle BW, Gibson, BE and Longmuir PE. 2012. Feasibility of improving the motor development of toddlers with congenital heart defects using a home-based intervention. *Cardiology in the Young* 33: 521-532.
DOI: 10.1007/s00246-011-0144-0.

Tabbutt S, Gaynor JW and Newburger JW. 2012. Neurodevelopmental outcomes after congenital heart surgery and strategies for improvement. *Current Opinion in Cardiology* 27: 82-91.
DOI: 10.1097/HCO.0b013e328350197b.

Tabbutt S. 2013. How to improve neurodevelopment and quality of life outcomes following early surgery for congenital heart disease? *Developmental Medicine & Child Neurology* 55: 1069–1074.
DOI: 10.1111/dmcn.12280.

Tahirović E, Begić H, Nurkić M, Tahirović H and Varni JW. 2010. Does the severity of congenital heart defects affect disease-specific health-related quality of life in children in Bosnia and Herzegovina? *European Journal of Paediatrics* 169: 349–353.
DOI 10.1007/s00431-009-1060-7.

Tak YR and McCubbin M. 2002. Family stress, perceived social support and coping following the diagnosis of a child's congenital heart disease. *Journal of Advanced Nursing* 39(2): 190–198.

Talwar S, Keshri VK, Choudhary SK and Airan B. 2015. Myocardial protection in neonates and infants: What have we learnt? Where do we go? *Journal of Heart and Circulation* 1(1): 105.
DOI: http://dx.doi.org/10.19104/jhc.2015.105.

Tantchou Tchoumi JC, Butera G, Giamberti A, Ambassa JC and Sadeu JC. 2011. Occurrence and pattern of congenital heart diseases in a rural area of sub-Saharan Africa. *Cardiovascular Journal of Africa* 22(2): 63-66.
DOI: CVJ-21.033.

Taylor CAL and Sarathchandra D. 2014. Socioeconomic position and low birth weight: Evaluating multiple and alternative measures across race in Michigan. *Social Sciences* 3: 549–564.
DOI: 10.3390/socsci3030549.

Tétreault S, Parrot A and Trahan J. 2003. Home activity programs in families with children presenting with global developmental delays: Evaluation and parental perceptions. *Journal of Rehabilitation Research* 26: 165–173.
DOI: 10.1097/01.mrr.0000088441.78481.56.

The *Lancet*. 2012. Editorial: A new milestone in the history of congenital heart disease. *The Lancet* 379(9835): 2401.
DOI: 10.1016/S0140-6736(12)61045-9.

Tikkanen AU, Oyaga AR, Riaño OA, Álvaro EM and Rhodes J. 2012. Paediatric cardiac rehabilitation in congenital heart disease: A systematic review. *Cardiology in the Young* 22(3): 241-50.
DOI: 10.1017/S1047951111002010.

Torowicz D, Irving SY, Hanlon AL, Fulbright Sumpter D and Medoff-Cooper B. 2010. Infant temperament and parent stress in 3-month old infants following surgery for complex congenital heart disease. *Journal of Developmental & Behavioural Paediatrics* 31(3): 202–208.
DOI: 10.1097/DBP.0b013e3181d3deaa.

Turer AT and Hill JA. 2010. Pathogenesis of myocardial ischaemia-reperfusion injury and rationale for therapy. *American Journal of Cardiology* 106(3): 360–368.
DOI: 10.1016/j.amjcard.2010.03.032.

United Nations International Children's Emergency Fund (UNICEF). 2013. Key facts and figures on nutrition.
(http://www.unicef.org/iran/Facts_and_Figures_on_Nutrition(2).pdf)
Retrieved on 29 August 2016.

United Nations International Children's Emergency Fund -World Health Organisation-World Bank (UNICEF-WHO-WB). 2015. Levels and trends in child malnutrition. UNICEF – WHO – World Bank Group joint child malnutrition estimates. Key findings of the 2015 edition.
(http://reliefweb.int/report/world/levels-and-trends-child-malnutrition-unicef-who-world-bank-group-joint-child)
Retrieved on 29 August 2016.

United States (US)-Department of Health and Human Services. 2014. Healthy People 2020.
(http://www.healthypeople.gov/2020/about/foundation-health-measures/Health-Related-Quality-og-Life-and-Well-Being)
Retrieved on 10 August 2015.

Uzark K and Jones K. 2003. Parenting stress and children with heart disease. *Journal of Paediatric Healthcare* 17(4): 163-168.
DOI: 10.1067/mph.2003.22.

Uzark K, Jones K, Burwinkle TM and Varni JW. 2003. The Paediatric Quality of Life Inventory™ in children with heart disease. *Progress in Paediatric Cardiology* 18: 141-148.
DOI: 10.1016/S1058-9813(03)00087-0.

Uzark K, Jones K, Slusher J, Limbers CA, Burwinkle TM and Varni JW. 2008. Quality of life in children with heart disease as perceived by children and parents. *Paediatrics* 121(5): e1060-e1067.
DOI: 10.1542/peds.2006-3778.

Uzark K, King E, Spicer R, Beekman R, Kimball T and Varni JW. 2013. The clinical utility of health-related quality of life assessment in paediatric cardiology outpatient practice. *Congenital Heart Disease* 8: 211–218.
DOI: 10.1111/chd.12002.

Vaidyanathan B, Nair SB, Sundaram KR, Babu UK, Shivapprakasha K, Rao SG and Kumar RK. 2008. Malnutrition in children with congenital heart disease (CHD): Determinants and short-term impact of corrective intervention. *Indian Paediatrics* 45: 541-546.

Van der Meer G and Loock JW. 2008. Why patients miss follow-up appointments: a prospective control-matched study. *East African Journal of Public Health* 5(3): 154-156.

Van Deventer JD, Doubell AF, Herbst PG, Piek H, Piek C, Marcos E and Pecoraro AJK. 2015. Evaluation of the SUNHEART Cardiology outreach programme. *SA Heart* 12:82-86.

Van Gameren-Oosterom HBM, Fekkes M, Buitendijk SE, Mohangoo AD, Bruil J and VanWouwe JP. 2011. Development, problem behaviour, and quality of Life in a population based sample of eight-year-old children with Down syndrome. *PLoS ONE* 6(7): e21879.
DOI: 10.1371/journal.pone.0021879.

Van Gameren-Oosterom HBM, VanDommelen P, Oudesluys-Murphy AM, Buitendijk SE, VanBuuren S and VanWouwe JP. 2012. Healthy growth in children with Down syndrome. *PLoS ONE* 7(2): e31079.
DOI: 10.1371/journal.pone.0031079.

Varan B, Tokel K and Yilmaz G. 1999. Malnutrition and growth failure in cyanotic and acyanotic congenital heart disease with and without pulmonary hypertension. *Archives of Disease in Childhood* 81: 49–52.

Varni JW, Seid M and Kurtin PS. 1999a. Paediatric health-related quality of life measurement technology: A guide for health care decision makers. *Journal of Clinical Outcomes Management* 6(4): 33-40.

Varni JW, Limbers CA and Burwinkle TM. 2007. Parent proxy-report of their children's health-related quality of life: an analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL™ 4.0 Generic Core Scales. *Health and Quality of Life Outcomes* 5: 2.
DOI: 10.1186/1477-7525-5-2.

Varni JW, Limbers CA, Neighbors K, Schulz K, Lieu JEC, Heffer RW, Tuzinkiewicz K, Mangione-Smith R, Zimmerman JJ and Alonso EM. 2011. The PedsQL™ Infant Scales: Feasibility, internal consistency reliability, and validity in healthy and ill infants. *Quality of Life Research* 20: 45–55.
DOI: 10.1007/s11136-010-9730-5.

Varni JW. 2013. Scaling and scoring of the Paediatric Quality of Life Inventory™ (PedsQL™). Lyon: Mapi Research Trust.

Versaw-Barnes D and Wood A. 2015. The infant at risk for developmental delay. In Tecklin JS (Ed.). *Paediatric Physical Therapy*. Fifth Edition. Philadelphia: Lippincott Williams and Wilkins p109.

Verster LJ. 2010 The Stress Levels of Parents whose Children are on Antiretroviral Therapy. (Unpublished MSc in Physiotherapy). University of Witwatersrand, Johannesburg.

Visootsak J, Mahle WT, Kirshbom PM, Huddleston L, Caron-Besch M, Ransom A and Sherman SL. 2011. Neurodevelopmental outcomes in children with Down syndrome and Congenital Heart Defects. *American Journal of Medical Genetics Part A* 155A(11): 2688–2691.
DOI: 10.1002/ajmg.a.34252.

Visootsak J, Hess B, Bakeman R and Adamson LB. 2013. Effect of congenital heart defects on language development in toddlers with Down syndrome. *Journal of Intellectual Disability Research* 57(9): 887–892.
DOI: 10.1111/j.1365-2788.2012.01619.x.

Visootsak J, Huddleston L, Buterbaugh A, Perkins A, Sherman S and Hunter J. 2015. Influence of CHDs on psychosocial and neurodevelopmental outcomes in children with Down syndrome. *Cardiology in the Young* pp 1-7
DOI: 10.1017/S1047951115000062

Vohr BR, Stephens BE, Higgins RD, Bann CM, Hintz SR, Das A, Newman JE, Peralta-Carcelen M, Yolton K, Dusick AM, Evans PW, Goldstein RF, Ehrenkranz RA, Pappas A, Adams-Chapman I, Wilson-Costello DE, Bauer CR, Bodnar A, Heyne RJ, Vaucher YE, Dillard RG, Acarregui MJ, McGowan EC, Myers GJ, Fuller J, for the *Eunice Kennedy Shriver* National Institute of Child Health and Network Human Development Neonatal Research. 2012. Are outcomes of extremely preterm infants improving? Impact of Bayley assessment on outcomes. *The Journal of Paediatrics* 161(2): 222–8.e3.
DOI: 10.1016/j.jpeds.2012.01.057.

Von Rhein M, Scheer I, Loenneker T, Huber R, Knirsch W and Latal B. 2011. Structural brain lesions in adolescents with Congenital Heart Disease. *Journal of Paediatrics* 158: 984-989.
DOI: 10.1016/j.jpeds.2010.11.040.

Von Rhein M, Dimitropoulos A, Valsangiacomo Buechel ER, Landolt MA and Latal B. 2012. Risk factors for neurodevelopmental impairments in school-age children after cardiac surgery with full-flow cardiopulmonary bypass. *Journal of Thoracic and Cardiovascular Surgery* 144: 577-583.
DOI: 10.1016/j.jtcvs.2012.02.005.

Vrijmoet-Wiersma CMJ, Ottenkamp J, VanRoozendaal M, Grootenhuis MA and Koopman HM. 2009. A multi-centric study of disease-related stress, and perceived vulnerability, in parents of children with congenital cardiac disease. *Cardiology in the Young* 19: 608–614.
DOI: 10.1017/S1047951109991831.

Walker SP, Wachs TD, Meeks Gardner J, Lozoff B, Wasserman GA, Pollitt E, Carter JA and the International Child Development Steering Group. 2007. Child development: risk factors for adverse outcomes in developing countries. *The Lancet* 369: 145–57.
DOI: 10.1016/S0140-6736(07)60076-2
Wang Y and Chen H-J. 2012. Use of percentiles and z-scores in anthropometry. In Preedy VR (Ed.). *Handbook of Anthropometry: Physical Measures of Human Form in Health and Disease.* New York: Springer pp 29-48.

Ward C, Makusha, and Bray R. 2015. Parenting, poverty and young people in South Africa: What are the connections? In *South African Child Gauge 2015.* Part 2: Youth and the intergenerational transmission of poverty pp 69- 74.
(http://www.ci.org.za/depts/ci/pubs/pdf/general/gauge2015/Child_Gauge_2015-Parenting.pdf)
Retrieved on 02 September 2016.

Weakliem DL and Adams J. 2011. What Do We Mean by “Class Politics”? *Politics & Society* 39: 475-495.

Weedon M and Potterton J. 2011. Socio-economic and clinical factors predictive of paediatric quality of life post burn. *Burns* 37: 572–579.
DOI: 10.1016/j.burns.2010.12.002.

Wei H, Roscigno CI, Swanson KM, Black BP, Hudson-Barr D, and Hanson CC. 2016. Parents' experiences of having a child undergoing congenital heart surgery: An emotional rollercoaster from shocking to blessing. *Heart & Lung* 45:154-160.
DOI: 10.1016/j.hrtlng.2015.12.007.

Werner H, Latal B, Valsangiacomo Buechel E, Beck I and Landolt MA. 2014. Health-related quality of life after open-heart surgery. *The Journal of Paediatrics*
64(2):254-258.
DOI: org/10.1016/j.jpeds.2013.10.022.

Wernovsky G. 2008. Improving neurologic and quality-of-life outcomes in children with congenital heart disease: Past, present, and future. *Journal of Thoracic and Cardiovascular Surgery* 135: 240-242.
DOI: 10.1016/j.jtcvs.2007.07.057.

Wheat JC. 2002. Nutritional Management of Children with Congenital Heart Disease. *Nutrition Bytes* 8(2).
(http://escholarship.org/uc/item/6jh767ps)
Retrieved on 28 April 2016.

Whitehead N, Potterton J and Coovadia A. 2014. The neurodevelopment of HIV-infected infants on HAART compared to HIV-exposed but uninfected infants. *AIDS Care* 26(4): 497–504.
DOI: 10.1080/09540121.2013.841828.

Wilmot I, Lorts A and Morales D. 2013. Paediatric mechanical circulatory support. *Korean Journal of Thoracic and Cardiovascular Surgery* 46(6): 391–401.
DOI: 10.5090/kjtcs.2013.46.6.391

Wong LP. 2008. Focus group discussion: A tool for health and medical research. *Singapore Medical Journal* 49(3): 256-261.

World Health Organisation (WHO). 1948. Preamble to the Constitution of the World Health Organisation as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) entered into force on 7 April 1948.
(http://www.who.int/about/definition/en/print.html)
Retrieved on 24 April 2016.

World Health Organisation (WHO). 2001. International Classification of Functioning, Disability and Health (ICF). Geneva: WHO.
(http://www.who.int/classifications/icf/en/)
Retrieved on 24 April 2016.

World Health Organisation (WHO) 2006. Multi-centre Growth Reference Study Group. WHO Child Growth Standards: Length/ height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva, World Health Organization.
(http://www.who.int/childgrowth/standards/Technical_report.pdf?ua=1)
Retrieved on 15 May 2016.

World Health Organisation (WHO) 2006. Multicentre Growth Reference Study Group. Assessment of sex differences and heterogeneity in motor milestone attainment among populations in the WHO Multicentre Growth Reference Study. *Acta Paediatrica* Supplement. 2006. p. 66-75.

World Health Organisation (WHO). 2007. International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) Geneva: WHO.
(http://www.who.int/classifications/icf/en/)
Retrieved on 24 April 2016.

World Health Organisation (WHO). 2015. World Health Statistics 2015.
(http://apps.who.int/iris/bitstream/10665/170250/1/9789240694439_eng.pdf?ua=1)
Retrieved on 26 August 2016.

Wilson WM, Smith-Parrish M, Marino BS and Kovacs AH. 2015. Neurodevelopmental and psychosocial outcomes across the congenital heart disease lifespan. *Progress in Paediatric Cardiology* 39: 113-118.
DOI: org/10.1016/j.ppedcard.2015.10.011.

Wypij D, Newburger JW, Rappaport LA, du Plessis AJ, Jonas RA, Wernovsky G, Lin M and Bellinger DC. 2003. The effect of duration of deep hypothermic circulatory arrest in infant heart surgery on late neurodevelopment: The Boston Circulatory Arrest Trial. *The Journal of Thoracic and Cardiovascular Surgery* 126(5): 1397-1403.
DOI: 10.1016/S0022-5223(03)00940-1.

Yildiz A, Celebioglu A and Olgum H. 2009. Distress levels in Turkish parents of children with congenital heart disease. *Australian Journal of Advanced Nursing*
26(3): 39-46.
(http://www.ajan.com.au/Vol26/26-3_Celebioglu.pdf)
Retrieved on 12 February 2013.

Zarit SH, Reever KE and Bach-Peterson J. 1980. Relatives of the impaired elderly: correlates of feelings of burden. *The Gerontologist* 20(6): 649-55.
DOI: 10.1093/geront/20.6.649.

Zemel BS, Pipan M, Stallings VA, Hall W, Schadt K, Freedman DS and Thorpe P. 2015. Growth Charts for children with Down syndrome in the United States. *Paediatrics* 136(5): e1204-e1211.
DOI: 10.1542/peds.2015-1652.

Zühlke L. 2013. Challenges and opportunities in paediatric cardiac services: Time for action. *SA Heart* 10(2): 431-433.

Zühlke L, Mirabel M and Marijon E. 2013. Congenital heart disease and rheumatic heart disease in Africa: recent advances and current priorities. *Heart* 0:1–8.
DOI: 10.1136/heartjnl-2013-303896.

APPENDICES

APPENDIX I

CLASSIFICATION OF CONGENITAL HEART DISEASE BASED ON THE NATURE OF THE DEFECT

APPENDIX I

CLASSIFICATION OF CONGENTIAL HEART DISEASE BASED ON THE NATURE OF THE DEFECT

Table I.1 Classification of acyanotic congenital heart disease

Diagnosis	Nature of defect	Intervention required	Outcome
Acyanotic cardiac defects			
PDA	The vascular connection between the pulmonary truncus and the aorta fails to close after birth.	Cardiac catheterisation or cardiac surgery for repair.	Excellent.
ASD	Abnormal opening in the atrial septum allowing the communication of blood between the left and right atrium.	Cardiac catheterisation or cardiac heart surgery for repair.	Excellent.
VSD	Abnormal opening in ventricular septum allowing the communication of blood between the left and right ventricle.	Cardiac catheterisation or cardiac surgery for repair.	Excellent.
AVSD	Central defect in the atrioventricular septum due to incomplete fusion of the tendocardial cushions, the membranous portion of the ventricular septum and the septal leaflets of the tricuspid and mitral valves.	Cardiac surgery for repair.	Excellent.
AS	Narrowing of the aortic valve resulting in obstruction to blood flow from the left ventricle.	Cardiac catheterisation or cardiac surgery for repair.	Excellent.
PS	Narrowing of the pulmonary valve resulting in obstruction to blood flow from the right ventricle	Cardiac catheterisation or cardiac surgery for repair.	Excellent.
Coarctation of the aorta	Congenital narrowing of the aorta as it leaves the heart in the segment of the aorta just after the arteries to the head and upper limb branch off	Cardiac surgery for repair.	Excellent.

(Adapted from Hanson, 2015; Morrow, 2012; Starr and Tucker, 2005).

Table I.2 Classification of cyanotic congenital heart disease

Diagnosis	Nature of lesion	Intervention required	Outcome
CYANOTIC CARDIAC DEFECTS			
TOF	Characterised by a high riding VSD, right ventricular hypertrophy, and pulmonary stenosis anomalous position of aorta.	Staged cardiac surgery. Early palliation and staged repair.	Excellent.
HLHS	Hypoplasia or absence of the left ventricle, and hypoplasia of the ascending aorta.	Staged cardiac surgery for palliation Early palliation and later repair. If palliation fails will require cardiac transplant.	Poorest of all defects.
TGA and DORV	Aorta arises from the right ventricle and the pulmonary artery from the left ventricle. In the case of DORV, the aorta and pulmonary artery both arise from the right ventricle.	Staged cardiac surgery for palliation in the neonatal phase and early surgical correction via arterial switch procedure.	Excellent.
Interrupted aortic arch	Faulty development of aortic arch system, the segment between left common carotid artery and the subclavian artery is absent. Usually associated with VSD shunting.	Cardiac surgery to reconstruct and reconnect the aortic arch and close VSD.	Excellent.
TAPVR	Pulmonary venous blood return is to the right atrium or systemic veins instead of the left atrium.	Cardiac surgery for repair.	Excellent.
Tricuspid atresia	The tricuspid valve fails to develop.	Staged cardiac surgery for palliation then surgery for repair.	Excellent.
Pulmonary atresia	The pulmonary valve fails to develop	Cardiac catherisation and staged cardiac surgery for palliation and later repair.	Excellent.
Truncus arteriosus	Combined pulmonary artery and aorta, often accompanied by a VSD.	Cardiac surgery.	Excellent.

(Adapted from Hanson, 2015; Morrow, 2012; Starr and Tucker, 2005).

APPENDIX II

CLASSIFICATION OF CONGENITAL HEART DISEASE BASED ON MEDICAL SEVERITY

APPENDIX II

CLASSIFICATION OF CONGENITAL HEART DISEASE BASED ON MEDICAL SEVERITY

Table II.1 Cardiologist's perception of medical severity scale

Grading	Description
1	Mild disorder requiring no therapy or effectively treated without surgery via cardiac catheterisation. Long-term follow up indicated.
2	Moderate disorder, the child is asymptomatic. Requires surgical correction (curative) or requires no therapy. The defect is easily repaired.
3	Marked disorder, and the child is symptomatic. Surgical repair, which is often difficult, will be required (one or more procedures). Often-significant residual effects or need for further surgery.
4	Severe disorder that is not correctable or requires complex palliative repair.

(Yildiz et al., 2009; Uzark et al., 2003; DeMaso et al., 1991).

APPENDIX III
USER AGREEMENT WITH PEARSON, INC. FOR THE BSID-III

APPENDIX III

USER AGREEMENT FOR THE BSID-III

Dear Robyn,

Permission to use a Pearson assessment is inherent in the qualified purchase of the test materials in sufficient quantity to meet your research goals. In any event, Pearson has no objection to you using the Bayley Scales of Infant and Toddler Development™, Third Edition (Bayley-III) and **you may take this email response as formal permission from Pearson to use the test in its as-published formats in your student research**.

If you do not yet qualify to purchase the test, your professor or faculty supervisor may be able to assist you by lending their qualifications and supervising your use of the test.

The BAYLEY-III is a sensitive clinical assessment that requires a high degree (CL2) to purchase, administer, score and interpret. It also represents Pearson copyright and trade secret material. As such, Pearson **does not permit photocopying or other reproduction of our test materials by any means and for any purpose when they are readily available in our catalog. Consequently, you may not simply reproduce the Bayley-III test forms**.

Long term license agreements with our Test Authors prohibit Pearson from providing or licensing our test materials at no charge/gratis for any purpose. As a resident of South Africa, to qualify for and purchase additional Bayley-III test materials, please visit the following link to the product page in our Pearson Assessment UK online catalog:
http://www.pearsonclinical.co.uk/Psychology/ChildCognitionNeuropsychologyandLanguage/ChildGeneralAbilities/BayleyScalesofInfantandToddlerDevelopmentThirdEdition(Bayley-III)/BayleyScalesofInfantandToddlerDevelopmentThirdEdition(Bayley-III).aspx

Finally, because of test security concerns, permission is not granted for appending tests to theses, dissertations, or reports of any kind. You may not include any actual assessment test items, discussion of any actual test items or inclusion of the actual assessment product in the body or appendix of your dissertation or thesis. You are only permitted to describe the test, its function and how it is administered and discuss the fact that you used the Test, your analysis, summary statistics, and the results.

Regards,

William H. Schryver

William H. Schryver
Senior Licensing Specialist
Pearson
Always Learning
Learn more at www.psychorp.com
Please respond only to pas.licensing@pearson.com

APPENDIX IV
USER AGREEMENT WITH PAR, INC. FOR THE PSI-SF

APPENDIX IV
USER AGREEMENT FOR THE PSI-SF

PAR
Creating Connections. Changing Lives.

16204 N. FLORIDA AVENUE • LUTZ, FLORIDA 33549
Telephone: 813.968.3003 • Fax: 813.968.2598 • Web: www.parinc.com

Sent Via Email: SmithRobyn@ufs.ac.za

November 12, 2013

Mrs. Robyn Smith
University of Free State, Bloemfontein, South Africa
CR de Wet Building, Rectors Road
Main Campus, Nelson Mandela Drive
Bloemfontein, Free State
9301 SOUTH AFRICA

Dear Mrs. Smith:

This letter is to confirm that Psychological Assessment Resources, Inc. (PAR) is willing to grant Mrs. Robyn Smith permission to use the PSI-SF in English, Afrikaans and Sesotho in her research study titled: *Neurodevelopment, quality of life and burden of care of young children who have undergone cardiac interventions in Central South Africa.*

Use of the PSI-SF is only permitted after the PSI-SF in English has been purchased and a Permission Agreement has been fully executed and paid for use of the PSI-SF in Afrikaans and Sesotho.

Sincerely,

Vicki King
Executive Assistant
to the Chairman and CEO

APPENDIX V

USER AGREEMENT WITH MAPI RESEARCH TRUST FOR THE PedsQL™

APPENDIX V

USER AGREEMENT FOR THE PEDSQL™

Dear Robyn,

Thanks a lot for sending the signed documents. You will consequently find attached to this email the Infant scale module in US English, Afrikaans and Sesotho as well as the template and the linguistic validation guidelines for the translation of the Cardiac Module. I am also attaching the Scoring Manual for this Questionnaire.

I would be most grateful if you could please kindly confirm safe reception. Many anticipated thanks. Please note that the backward translations of the cardiac module must by reviewed by the author for approval. Therefore ready I invite you to provide Mapi with them.

You can consider this message as an authorization to use the PedsQL Questionnaire in your study. Please do not hesitate to get back to me should you have any question or need anything else.

Kind regards,
Piero

Piero Bindi
Information Resources Specialist
PROs & ClinROs Information Support Unit

Mapi Research Trust
27 rue de la Villette | 69003 LYON | FRANCE
Tel: +33 (0) 4 72 13 65 75 | Tel: +33 (0) 4 72 13 59 86 (Direct Line)

APPENDIX VI

ETHICAL CLEARANCE CERTIFICATES

APPENDIX VI
ETHICAL CLEARANCE CERTIFICATES

ETHICAL CLEARANCE FROM THE ETHICS COMMITTEE OF THE FACULTY OF HEALTH SCIENCES, UNIVERSITY OF THE FREE STATE

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA
UFS UV

[redacted]

Research Division
Internal Post Box G40
☎(051) 4052812
Fax (051) 4444359
Ms H Strauss/hv

E-mail address: StraussHS@ufs.ac.za

2013-11-07

REC Reference nr 230408-011
IRB nr 00006240

MS R SMITH
DEPARTMENT OF PHYSIOTHERAPY
CR DE WET BUILDING
UFS

Dear Ms Smith

ECUFS NR 177/2013
MS R SMITH **DEPARTMENT OF PHYSIOTHERAPY**
UNIVERSITY OF THE WITWATERSRAND

PROJECT TITLE: NEURODEVELOPMENT, QUALITY OF LIFE AND BURDEN OF CARE OF YOUNG CHILDREN WHO HAVE UNDERGONE CARDIAC INTERVENTIONS IN CENTRAL SOUTH AFRICA: SIX WEEK AND SIX MONTH POST CARDIAC INTERVENTION OUTCOMES.

- You are hereby kindly informed that the Ethics Committee approved the above project at the meeting held on 5 November 2013.

  [Mrs Smith did not take part in the discussion of this study]

- Committee guidance documents: Declaration of Helsinki, ICH, GCP and MRC Guidelines on Bio Medical Research. Clinical Trial Guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles Structure and Processes Department of Health RSA 2004; Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa, Second Edition (2006); the Constitution of the Ethics Committee of the Faculty of Health Sciences and the Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines.

- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

- The Committee must be informed of any serious adverse event and/or termination of the study.

- All relevant documents e.g. signed permission letters from the authorities, institutions, changes to the protocol, questionnaires etc. have to be submitted to the Ethics Committee before the study may be conducted (if applicable).

- A progress report should be submitted within one year of approval of long term studies and a final report at completion of both short term and long term studies.

- Kindly refer to the ETOVS/ECUFS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully



DR SM LE GRANGE
ACTING CHAIR: ETHICS COMMITTEE

Cc Dr J Potterton

ETHICAL CLEARANCE FROM THE HUMAN RESEARCH ETHICS (MEDICAL) COMMITTTE, UNIVERSITY OF THE WITWATERSRAND

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M131056

NAME: (Principal Investigator)	Mrs Robyn Smith
DEPARTMENT:	Department of Physiotherapy Medical School
PROJECT TITLE:	Neurodevelopment, Quality of Life and Burden of Care of Young Children Who Have Undergone Cardiac Interventions in Central South Africa: Six Week and Six Month Post Cardiac Intervention Outcomes
DATE CONSIDERED:	25/10/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Joanne Potterton
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 25/11/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature M131056Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX VII

PERMISSION LETTERS FROM RELEVANT AUTHORITIES

APPENDIX VII

PERMISSION LETTERS FROM RELEVANT AUTHORITIES

health
Department of Health
FREE STATE PROVINCE

20 September 2013

Ms. Robyn Smith
Department of Physiotherapy
School of Allied Health Sciences
University of the Free State

Dear Ms Smith

RESEARCH PROJECT: NEURODEVELOPMENT, QUALITY OF LIFE AND BURDEN OF CARE OF YOUNG CHILDREN WHO HAVE UNDERGONE CARDIAC INTERVENTIONS IN CENTRAL SOUTH AFRICA: SIX WEEK AND SIX MONTH POST CARDIAC INTERVENTION OUTCOMES.

Herewith permission for the mentioned project to be done at Universitas Academic Hospital on the following conditions:

1. The research should not expose the users and the Department to any avoidable harm.
2. Annual progress reports should be submitted and also a research report at the end of the research process.
3. Reporting of Adverse Events related to the research process must be done within 48 hours of discovery.
4. There shall be provision for obtaining informed consent from all patients/staff where appropriate.
5. Briefing sessions should be conducted with all stakeholders prior to commencement and at the end of the study to provide feedback where appropriate.
6. That approval is obtained from the Ethics Committee.

The Chief Executive Officer must be notified if the findings of the project will be published and a research report needs to be sent to the Head Clinical Services as soon as the study is completed.

Yours sincerely

DR NRJ VAN ZYL
2013 -10- 04
HEAD: CLINICAL SERVICES
UNIVERSITAS ACADEMIC HOSPITAL

DR NIC R J VAN ZYL
HEAD: CLINICAL SERVICES
UNIVERSITAS ACADEMIC HOSPITAL

HEAD: CLINICAL SERVICES: DR NRJ VAN ZYL
Private Bag X20660, Bloemfontein, 9300. Tel. No.: 051-4052866,
Fax: 051-4053500, Room 1077, First Floor, Universitas Academic Hospital
Email: vanzylnr@universitas.fs.gov.za

Pediatriese Kardiologie

Tel: (051) 405 3302
faks/fax: (051) 444 3230

E-pos/Email
BuysDG@ufs.ac.za
GNPDSCB@ufs.ac.za

Paediatric Cardiology

339(G69), Bloemfontein, 9300
Suid Afrika / South Africa

Ref: 2013/83

ATTENTION:

Bloemfontein, 19 Sep 2013

R Smith
Physiotherapy
PO Box 339, UFS
Bloemfontein, 9300

FROM:

Prof SC Brown

Dear Robyn

STUDY: NEURODEVELOPMENT, QoL AND BURDEN OF CARE OF YOUNG CHILDREN UNDERGOING CARDIAC INTERVENTION IN CENTRAL SOUTH AFRICA: SIX WEEK AND SIX MONTH OUTCOMES

I hereby give permission for the above mentioned study to be conducted in the department of Paediatric Cardiology, Universitas Hospital. We shall allow you access to all the information required for the study.

Please note that this is based on approval from the local ethics committee and CEO of hospital.

many regards

Prof SC Brown M.Med
Prin Specialist Peadiatrics
MP: 0270954 • Tel nr: 405 3241

UNIVERSITY OF THE
FREE STATE
UNIVERSITEIT VAN DIE
VRYSTAAT
YUNIVESITHI YA
FREISTATA

UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

19 September 2013

Me Robyn Smith
Lecturer
Dept of Physiotherapy
University of the Free State
P O Box 339
Bloemfontein
9300

Dear Me Smith

PERMISSION TO CONDUCT STUDY IN DEPT CARDIOTHORACIC SURGERY, UNIVERSITAS ACADEMIC HOSPITAL, BLOEMFONTEIN

Hereby I, in my capacity as Head of the Departement Cardiothoracic Surgery, give permission that the study, titled: "Neurodevelopment, quality of life and burden of care of young children who have undergone cardiac interventions in central South Africa: Six week and six month post cardiac intervention outcomes" can be conducted in our Department.

Regards

PROF FRANCIS E SMIT
HEAD: DEPT CARDIOTHORACIC SURGERY

APPENDIX VIII

PARENT INFORMATION LETTER AND INFORMED CONSENT FORM: PHASE I AND II

APPENDIX VIII

PARENT INFORMATION LETTER AND INFORMED CONSENT FORM: PHASE I AND II

NEURODEVELOPMENT, QUALITY OF LIFE AND BURDEN OF CARE OF YOUNG CHILDREN WHO HAVE UNDERGONE CARDIAC INTERVENTIONS IN CENTRAL SOUTH AFRICA:
THREE-MONTH AND SIX-MONTH POST CARDIAC INTERVENTION OUTCOMES

Dear parent(s)/caregiver,

My name is Robyn Smith and I am a physiotherapist. I am currently doing research as part of my Doctorate of Philosophy (PhD) studies at the University of the Witwatersrand (WITS). Research is simply the process by which one finds the answers to a question.

Background and motivation

Congenital heart defects are the most common birth defect affecting children. It is a serious condition, and depending on how severe the defect is, it can hold the risk of associated problems including delayed development and neurological problems.

The ability to identify heart defects, and treat them at a young age has significantly improved over recent years. This has resulted in many more children now surviving and living into adulthood. It is becoming increasingly important to look at how children surviving heart defects are growing, developing and functioning in their everyday lives over time. It is also important to look at the quality of life of both the child and that of their family. This information is important to healthcare professionals in order for us to

evaluate the standard of our services and to continue to improve the care we provide to children with heart conditions.

To date very little research has been done, particularly in South Africa, regarding how children surviving heart defects are doing over time. There has also been no research regarding the benefit of early and continued developmental evaluation and the implementation of a home-based, parent-driven developmental stimulation programme in improving developmental outcome of children with congenital heart defects.

Aim of the study

I wish to determine your child's development and quality of life before their cardiac intervention, at three months after their cardiac intervention and again at six months after their cardiac intervention. I will be looking at changes in your child's development and quality of life over this period of time.

I also wish to look at identifying possible risk factors for poor developmental outcome in South African children. I am also extremely interested in finding out how caring for a child with a congenital heart defect affects you and your family life, and how this contributes to the level of stress you are experiencing.

Finally I hope to use the information I gather about the developmental difficulties experienced by children with congenital heart defects, to help me develop a home-based, parent-driven developmental stimulation programme that will best address the needs of children with congenital heart defects.

If your child meets the necessary inclusion criteria, I would like to invite you and your child to participate in this study.

Format of the study

After you consent to participate in the study and provide permission for your child's participation an initial assessment will be scheduled to take place at one of your

routine cardiology clinic visits before any cardiac-intervention procedures take place. This baseline assessment will provide important information about your child's growth, development and quality of life before any cardiac intervention.

I will consult your child's medical record and talk to your cardiologist to gather information about your child's condition and treatment. I will then interview you, the parent(s)/caregiver, in order to gather important information about your family and how caring for your child is impacting on your life. You will also be asked to complete two (2) brief questionnaires, one relating to the levels of stress you are currently experiencing, and one regarding your view of your child's quality of life.

I will then do a physical assessment which will include looking at your child's vital signs (heart rate, breathing rate, blood pressure and levels of oxygen in their blood), growth (length, weight and head circumference) as well as doing a comprehensive assessment of your child's development. The first assessment will take approximately one to one and a half hours to complete.

Your child will then undergo cardiac intervention which may be open heart surgery or an interventional catheter-based cardiology procedure. Upon discharge following the intervention I will schedule a follow-up appointment for three months after the procedure. I will contact you telephonically three days beforehand to remind you of your appointment.

At your three-month follow-up visit I will again assess your child's vital signs, growth and development. You will again be asked to complete the same two (2) brief questionnaires as with the first assessment, and I will again ask about the burden of care. This visit will take approximately one hour. At the end of this visit I will schedule a follow-up appointment for six months after your child's initial cardiac intervention. I will contact you telephonically three days beforehand to remind you of your appointment.

At your six month follow-up I will again assess your child's vital signs, growth and development. You will again be asked to complete the same two (2) brief

questionnaires as with the first assessment, and I will again ask about the burden of care. This visit will take approximately one hour.

Where ever possible follow-up appointments will be scheduled to coincide with your normal clinic visits to minimise any inconvenience, or as suitable to your schedule. If you are unable to attend a scheduled appointment I will request that you telephonically contact the researcher to reschedule your appointment as soon as is possible for you.

The information gathered from these assessments will be used to determine the type of developmental problems experienced by children with congenital heart defects. I will then use this information to assist me in developing guidelines for a developmental stimulation programme aimed at addressing these specific needs.

After the completion of the initial part of the study you may subsequently be invited to participate in a group session aimed at evaluating whether such a home-based developmental stimulation programme would adequately meet your needs.

Benefit of participating in the study

Your child may not directly benefit from their participation in this study. Participation in this study will in no way influence the standard care your child receives.

You will however have the benefits of regular, comprehensive assessment of your child's development and quality of life.

Your participation will help determine the developmental needs of young children living with congenital heart disease in central South Africa. This information will assist me developing a home-based, parent-driven developmental stimulation programme that specifically addresses the needs of these children.

Following the completion of the study if I identified any developmental concerns or your child requires any neurodevelopmental therapy your child will be referred accordingly to early intervention rehabilitation services.

Ethical considerations

This study holds no anticipated risk to you or your child. The assessments will be done in the Cardiology Department, Universitas Academic Hospital where medical personnel will be present. The physiotherapist is also experienced in working with children.

Your participation as well as that of your child in this study is voluntary, you may decline to participate or withdraw yourself and your child from the study at any point without the risk of discrimination or penalty. Your child will continue to receive standard care irrespective of your participation in the study.

You will not be remunerated for your participation in the study, but the researcher will reimburse you for your travelling costs for visits directly related to your participation in this study. An amount of R150 per visit will be provided per visit for transport. There are no additional costs to you personally for participating in the study.

All information about you and your child will be treated as confidential, only the researcher and your doctors will have access to this information. Complete confidentiality cannot however be guaranteed, as this information may be required to be disclosed if requested by a court of law or an ethics committee review.

Feedback on study outcome

The results of the study can be requested from the researcher following the completion of the study.

Presentation and publication of research findings

The results of the study may be used in presentations at academic congresses or in print in the form in an accredited journal. In the above cases all data pertaining to participants will be presented in an anonymous manner and no individual will be identifiable.

Ethical inquiries

This protocol has been reviewed by two ethics committee. If you have any questions or concerns pertaining to the ethical aspects of the study you may contact the researcher or the secretariats of the following ethics committees:

Ethics Committee of the Faculty of Health Sciences, University of Free State
Office of secretariat 051-4052812
StraussHS@ufs.ac.za

Medical Human Research Ethics Committee, University of Witwatersrand
Office of secretariat 011-7171234
anisa.keshav@wits.ac.za

If you have any inquiries, questions or concerns the researcher can be contacted at the following numbers:

Robyn Smith
Lecturer /Physiotherapist
Department of Physiotherapy
University Free State

051- 4013303 (w)
082 925 9367 (cell)

INFORMED CONSENT

I ....., have been informed about the study by the researcher, Mrs. Robyn Smith.

I ..... agree to participate in this study.

I hereby also grant permission that my child..... may participate in this study.

I am aware that our participation is voluntary, and that we can decline participation or withdraw from the study at any point without risk of penalty. I am aware that my child will continue to receive standard care irrespective of our participation.

I hereby agree that Robyn Smith may assess my child and have access to his/her medical information.

I am aware that I will only receive compensation of R150 per visit for our travelling costs for visits directly relating to our participation in this study.

I agree to attend the visits with my child as scheduled by Mrs. Smith.

I am aware that if any developmental concerns or problems are identified by Mrs. Smith during the course of the study my child will be referred to the appropriate rehabilitation services.

I have been informed that I may enquire about the study if I feel it is indicated, from either the researcher, Ms Smith or the secretariat of the ethics committees at the numbers provided in the information letter.

I am aware that I can request the results of the study upon its completion.

I am aware that the results of the study may be presented at academic congresses or in print in the form in a journal. I am aware that all our personal information will be treated as confidential and all results will be presented in an anonymous manner.

I am aware that following my participation in this the first part of the study I may later be invited to participate in parent/caregiver group sessions to evaluate whether the home-based, parent-driven developmental stimulation programme that is going to be developed will meet my specific needs as a parent/caregiver.

I am aware that I will be provided with a copy of the information letter and the signed copy of the informed consent for personal reference.

Signature of the parent/caregiver _____

Name in print _____

Date _____

Signature of the researcher _____

Name in print _____

Date _____

Signature of a witness _____

Name in print _____

Date _____

Signature of a translator _____

(If applicable)

Name in print _____

Date _____

APPENDIX IX

DATA FORM:

DEMOGRAPHIC INFORMATION OF THE CHILD AND FAMILY

APPENDIX IX

DATA FORM: DEMOGRAPHIC INFORMATION OF THE CHILD AND FAMILY

Subject number | C | | | |

Demographic data parent/caregiver

Maternal age at birth of the child | | | (y y)

Number of siblings | | |

Do any of your other children also have heart defects?

- ☐ Yes
- ☐ No
- ☐ Not applicable

If you are the child's mother please indicate if you had any of the following conditions during your pregnancy

- ☐ Diabetes mellitus
- ☐ Overweight/obesity
- ☐ Infections e.g. Rubella, toxoplasmosis
- ☐ Unknown

Residence of Parent/ Caregiver where child resides

- ☐ Bloemfontein
- ☐ Kimberley
- ☐ Maseru
- ☐ Other
- ☐ If other, specify _____

Ethnicity of the child

- ☐ Black
- ☐ White
- ☐ Coloured
- ☐ Asian
- ☐ If other, specify _____

What is your relationship with this child?

- ☐ Mother/ stepmother/ foster mother
- ☐ Father/ stepfather/ foster father
- ☐ Grandmother
- ☐ Grandfather
- ☐ Guardian
- ☐ If other , specify _____

What is your relationship with this child? (if a second person present)

- ☐ Mother/ stepmother/ foster mother
- ☐ Father/ stepfather/ foster father
- ☐ Grandmother
- ☐ Grandfather
- ☐ Guardian
- ☐ If other , specify _____

What language is spoken primarily in the home?

- ☐ English
- ☐ Afrikaans
- ☐ Sesotho
- ☐ Other, specify _____

Socio-economic status of the family

Highest level of education of mother/caregiver

- 7 ☐ Graduate of a professional degree
- 6 ☐ University graduate
- 5 ☐ Partial university/at one year specialised training
- 4 ☐ High school graduate
- 3 ☐ Grade 9-11
- 2 ☐ Grade 7- 8
- 1 ☐ Grade 6 and less
- 0 ☐ Not applicable/ unknown

Employment status of mother

- ☐ Employed full time
- ☐ Part-time employment
- ☐ Unemployed

Occupation/ job title mother _____

Occupational score mother

- 9 ☐ Executive, owner of large business, major professional
- 8 ☐ Administrators, lesser professionals, owner medium size business
- 7 ☐ Small business owner, owner farm, managers, minor professional
- 6 ☐ Technicians, small business owner, semi-professional
- 5 ☐ Clerical and sales worker, small farm and business owner
- 4 ☐ Smaller business, skilled labourer, craftsmen, tenant farmer
- 3 ☐ Machine operator, semi-skilled labourer
- 2 ☐ Unskilled worker
- 1 ☐ Farm labourer, menial worker, student, housewife
- 0 ☐ Not applicable/unknown

Highest level of education of father

7	☐	Graduate of a professional degree
6	☐	University graduate
5	☐	Partial university/ one year specialised training
4	☐	High school graduate
3	☐	Grade 9-11
2	☐	Grade 7- 8
1	☐	Grade 6 and less
0	☐	Not applicable/ unknown

Employment status of father

☐	Employed full time
☐	Part-time employment
☐	Unemployed

Occupation/ job title father _____

Occupational score mother /caregiver

9	☐	Executive, owner of large business, major professional
8	☐	Administrators, lesser professionals, owner medium size business
7	☐	Small business owner, owner farm, managers, minor professional
6	☐	Technicians, small business owner, semi-professional
5	☐	Clerical and sales worker, small farm and business owner
4	☐	Smaller business, skilled labourer, craftsmen, tenant farmer
3	☐	Machine operator, semi-skilled labourer
2	☐	Unskilled worker
1	☐	Farm labourer, menial worker, student, housewife
0	☐	Not applicable/unknown

Hollingshead socioeconomic status index mother/caregiver ☐

Hollingshead socioeconomic status index father ☐

Hollingshead socioeconomic status index family ☐

Social strata for the family

☐	55-66	major business and professional
☐	40-54	medium business, minor professional
☐	30-39	clerical, craftsmen, sales worker
☐	20-29	machinist, semi-skilled
☐	9-18	unskilled labour, menial worker

Birth history of child

Date of birth ☐☐☐☐☐☐
y y m m d d

Birthweight ☐☐☐☐ grams

Gestation ☐☐ weeks

Apgar Scores ☐/10 ☐/10

Impact of CHD on the family (burden of care)

In the last year has your child been hospitalised? Yes No

If so how many times ☐☐

Reason for these admissions _____
_____
_____

In the past month on how many days has your child been too ill to play/get up?
☐☐ days

In the past month on how many days did your child require special care?
due to his/her physical health ☐☐ days

If you work outside the home please answer the following questions
in the past month
How many days did you miss work due to your child's physical health?
☐☐ days

How often does your child's physical health affect your daily routine at work?
☐ Never
☐ Seldom
☐ Often
☐ Always

How often does your child's health affect your ability to concentrate at work?
☐ Never
☐ Seldom
☐ Often
☐ Always

References:

Hollingshead, AA.1975. Four factor index of social status. Unpublished manuscript, Yale University, New Haven, Conneticut

Varni, JW. 2008. PedsQL™ Family information form

APPENDIX X

DATA FORM:

CARDIAC DIAGNOSIS, AND MEDICAL AND SURGICAL MANAGEMENT

APPENDIX X
DATA FORM: CARDIAC DIAGNOSIS, AND MEDICAL AND SURGICAL MANAGEMENT

Subject number | C | | | |

Congenital heart defect Diagnostic information

Primary diagnosis _____
_____
_____

Diagnostic ICD-10-CM coding | | | | | | | | |

Child's HIV status
- ☐ Unknown
- ☐ HIV positive
- ☐ HIV negative

CHD classification
- ☐ Cyanotic
- ☐ Acyanotic

Severity of the heart defect
- ☐ Mild (requiring no therapy/effectively treated without surgery)
- ☐ Moderate (surgically corrected (curative) no therapy
- ☐ Moderate to severe (one or more surgery repair)
- ☐ Complex or severe disease uncorrectable or palliated

Age at which the defect was diagnosed? ☐☐ months

Age when treatment commenced? ☐☐ months

Mangement of the CHD to date (mark more than one option if indicated)
- ☐ No treatment required
- ☐ Conservative management including cardioactive drugs
- ☐ Cardiac catheterisation
- ☐ Surgery
- ☐ Other

If other, specify _____

Presence of any known extracardiac associations

Presence of known genetic syndromes associated with CHD

- ☐ None
- ☐ Down
- ☐ Edward
- ☐ Patau
- ☐ Turner
- ☐ Holt-oram
- ☐ Alagille
- ☐ Duchenne
- ☐ Barth
- ☐ Long QT
- ☐ DiGeorge
- ☐ Williams
- ☐ Noonan
- ☐ Marfan
- ☐ Kabuki
- ☐ Goldenhar
- ☐ Mitochondrial
- ☐ Pompes disease
- ☐ Hurler
- ☐ Other

If other, specify _____

Presence of structural malformations associated with CHD

- ☐ None
- ☐ CHARGE
- ☐ VACTERL
- ☐ Anorectal malformation
- ☐ Omphalocele
- ☐ Gastrochisis
- ☐ Tracheo-oesophageal fistula
- ☐ Renal abnormalities
- ☐ Congenital diaphragmatic hernia
- ☐ Muskuloskeletal abnormalities
- ☐ Other

If other, specify _____

Presence of any known teratogens (environmental risks) associated with CHD

- ☐ None
- ☐ Rubella
- ☐ Maternal diabestes
- ☐ Maternal obesity
- ☐ Smoking
- ☐ Vitamin A (acne treatment)
- ☐ Maternal alcohol consumption
- ☐ Smoking
- ☐ Phenylketonuria
- ☐ Other

If other, specify _____

Does the child have any central nervous system abnormalities?

- ☐ Yes
- ☐ No

If yes, specify the nature of abnormality

_____
_____
_____

Peri-operative Data (first surgery)

Did the child undergo any surgical intervention?

☐ Yes
☐ No

If yes, please complete the information below

Age at first surgery ☐☐ months

Date of the surgery ☐☐☐☐☐☐
y y m m d d

Aim of the surgery

☐ Palliation
☐ Staged correction
☐ Complete correction

Nature of the surgery/interventional procedure

_____
_____
_____

Surgical approach used

Median sternotomy ☐
Thoracotomy ☐
Other ☐
If other, specify _____

Surgical information:

Cardiopulmonary bypass	time	☐☐☐
Cross clamping aorta	time	☐☐☐
Hypothermic circulatory arrest	time	☐☐☐

Temperature during circulatory arrest ☐☐ degrees Celsius

Haematocrit ☐☐☐

Intensive Care admission

Did the child require pre-operative intubation and MV Yes | No

If yes, specify reason(s) _____
_____

Known neuromuscular weakness prior to ICU admission ☐ Yes ☐ No

If so, specify the nature of weakness _____
_____

Duration of invasive ventilation ☐☐☐ days

Did child require resuscitation at any point ☐ Yes ☐ No

Did child have any seizures ☐ Yes ☐ No

Number of days hospitalised upon discharge ☐☐☐ days

Was additional surgical intervention indicated at a later point in time ☐ Yes ☐ No

Peri-operative Data (second surgery)

Did the child undergo a second surgical procedure during the study period?

☐ Yes
☐ No

In summary, indicate if the child is at low or high risk for developmental delays or disorder based on the medical information gathered

☐ **High risk (need to meet the understated risk criteria)**
- ☐ Neonates or infants requiring open heart surgery (cyanotic or acyanotic lesions)
- ☐ Children with cyanotic lesions not requiring open heart surgery during infancy
- ☐ Any combination of CHD and any of the following co-morbidities
  - ☐ Prematurity
  - ☐ Developmental dealy recognised in infancy
  - ☐ Genetic syndrome associated with developmental difficulties
  - ☐ Cardiopulmonary resuscitation at any point
  - ☐ Prolonged hospitalisation (> 2 weeks) postoperatively
  - ☐ Perioperative seizures
  - ☐ Significant neuroimaging abnormalities or microcephaly
  - ☐ history of mechanical support

☐ **Low risk (none of the above mentioned risk criteria)**

APPENDIX XI

DATA FORM:

CARDIOVASCULAR, GROWTH AND NEUROMOTOR STATUS

APPENDIX XI
DATA FORM: CARDIOVASCULAR, GROWTH AND NEUROMOTOR STATUS

Subject number | C | | | |

ASSESSMENT 1: BASELINE

Cardiovascular status (vital signs)

Heart rate | | | | /min

Respiratory rate | | | | /min

Oxygen saturation | | | | %

Blood pressure ___/___ mmHg

Growth parameters

Weight | | | | | g

Height | | | | cm

Head circumference | | | | cm

Neuromotor status

Muscle tone
Hypotonic | |
Normal | |
Increased | |

Babinski — Left | postive | negative

Babinski — Right | postive | negative

Clonus — Left | postive | negative

Clonus — Right | postive | negative

ASSESSMENT 2: PHASE II (THREE-MONTHS POST INTERVENTION)

Cardiovascular status

Need for further cardiac interventions ☐ Yes ☐ No

Growth parameters

Weight ☐☐☐☐ g

Height ☐☐☐ cm

Head circumference ☐☐☐ cm

Neuromotor status

Muscle tone
Hypotonic ☐
Normal ☐
Increased ☐

Babinski
Left ☐ postive ☐ negative
Right ☐ postive ☐ negative

Clonus
Left ☐ postive ☐ negative
Right ☐ postive ☐ negative

ASSESSMENT 3: PHASE II (SIX-MONTHS POST INTERVENTION)

Cardiovascular status

Need for further cardiac interventions ☐ Yes ☐ No

Growth parameters

Weight ☐☐☐☐ g

Height ☐☐☐ cm

Head circumference ☐☐☐ cm

Neuromotor status

Muscle tone
Hypotonic ☐
Normal ☐
Increased ☐

Babinski
Left ☐ postive ☐ negative
Right ☐ postive ☐ negative

Clonus
Left ☐ postive ☐ negative
Right ☐ postive ☐ negative

APPENDIX XII

DATA FORM:

BURDEN OF CARE INFORMATION AT THREE-MONTH AND SIX-MONTH POST CARDIAC INTERVENTION

APPENDIX XII
DATA FORM: BURDEN OF CARE INFORMATION AT THREE-MONTH AND SIX-MONTH POST CARDIAC INTERVENTION

Subject number | P | | | |

BURDEN OF CARE THREE MONTHS POST CARDIAC INTERVENTION

Since your discharge following the cardiac intervention procedure, has your child been hospitalised? | Yes | No |

If so how many times | | |

Reason for these admissions _____
_____
_____

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, until now how many days has your child been too ill to play/get up?
| | | days

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, how many days did your child require special care due to his/her physical health?
| | | days

If you work outside the home please answer the following questions *in the past month*

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, How many days did you miss work due to your child's physical health?
| | | days

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, How often does your child's physical health affect your daily routine at work?

| | Never
| | Seldom
| | Often
| | Always

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, How often does your child's health affect your abilty to concentrate at work?

| | Never
| | Seldom
| | Often
| | Always

BURDEN OF CARE SIX MONTHS POST CARDIAC INTERVENTION

Since your discharge following the cardiac intervention procedure, has your child been hospitalised? | Yes | No |

If so how many times | | |

Reason for these admissions _____
_____
_____

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, until now how many days has your child been too ill to play/get up?
| | | days

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, how many days did your child require special care due to his/her physical health?
| | | days

If you work outside the home please answer the following questions
in the past month

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, How many days did you miss work due to your child's physical health?
| | | days

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, How often does your child's physical health affect your daily routine at work?

| | Never
| | Seldom
| | Often
| | Always

Since your discharge following your child's cardiac intervention procedure 6 weeks ago, How often does your child's health affect your abilty to concentrate at work?

| | Never
| | Seldom
| | Often
| | Always

References:

Varni, JW. 2008. PedsQL™ Family information form

APPENDIX XIII

DATA FORM:

PATH THROUGH THE STUDY

APPENDIX XIII
DATA FORM: PATH THROUGH THE STUDY

Subject number | C | | | |

Phase I : Pre- cardiac intervention status (baseline)

Interview and assessment done | Yes | No |

Date of assessment | | | | | | | |
d d m m y y

If you indicated No, why did the assessment not take place ?

	Loss to follow-up	_____
	Non-compliance	_____
	Mortality	_____
	Critical illness	_____
	Other	

If other, specify _____
_____
_____

Phase II: Three-month follow-up

Interview and assessment done | Yes | No |

Date of assessment | | | | | | | |
d d m m y y

If you indicated No, why did the assessment not take place ?

	Loss to follow-up	_____
	Non-compliance	_____
	Mortality	_____
	Critical illness	_____
	Other	

If other, specify _____
_____
_____

Phase II: Six month follow-up

Interview and assessment done

Yes
No

Date of assessment

d	**d**	**m**	**m**	**y**	**y**

If you indicated No, why did the assessment not take place ?

	Loss to follow-up	_____
	Non-compliance	_____
	Mortality	_____
	Critical illness	_____
	Other	

If other, specify _____
_____
_____

APPENDIX XIV
REGRESSION ANALYSIS:
VARIABLES PREDICITIVE OF KEY OUTCOMES

APPENDIX XIV
REGRESSION ANALYSIS:
VARIABLES PREDICTIVE OF KEY OUTCOMES

A regression analysis was done to determine variables that were predictive of key outcomes in development (cognitive, language and motor), HRQOL and parenting stress at all three time points of assessment (baseline, and three-months and six months post cardiac intervention). The regression analysis was done using two-way analysis of variance (ANOVAs). The regression analysis provides t-statistics and probabilities for coefficients, and only one F-statistic and probability for the regression. The coefficient of determination is listed as adjusted R-squared (R^2) and indicates the percentage of the variable on the left side of the equation that can be explained by the predictors. The-F-statistic tests whether the combination of predictors explains variation in the variable on the left side of the equation in a manner that is unlikely to occur by chance if the null hypothesis is true. P-values are provided for the F-test.

A linear regression model was used for each of the key outcome namely neurodevelopment (cognitive, motor and language), HRQOL and parenting stress. The effects used were the subcategories under each outcome. Interaction effects were also tested where appropriate. The code for the Anova models used was as follows:

General format: Variable (base, 3 months, 6 month) ~ Effect1 + Effect2 +....
Type and severity of CHD: Score ~ Severity + CHDtype + interaction of Severity:CHDtype
Surgery and medical course: Score ~ Age + CPBtime + POComplication + mechanic ventilation
Hospital and ICU length of stay: Score ~ ICU stay + Hospital stay
Patient factors: Score ~ Gender + Premature + Weight + DS + Growth
Sociodemographic factors: Score ~ Distance + Age + Education + SE status

VARIABLES PREDICTIVE OF NEURODEVELOPMENTAL OUTCOME

Cognitive development

Table XIV.1: Variables predictive of BSID-III cognitive scores at baseline

BSID-III cognitive scores (Baseline)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	-48.5	17.46	-2.79	0.01 **	0.19	0.03*
Type CHD	-23.33	12.51	-1.87	0.07		
Surgery an medical course						
Age at first surgery	-1.01	0.63	-1.63	0.12	-0.05	0.59
CPB time	0.05	0.65	0.70	0.49		
Postop complications	-2.61	10.55	-0.25	0.81		
Duration of MV	7.09	13.97	0.51	0.62		
Hospital and ICU length of stay						
ICU LOS	1.32	1.09	1.21	0.23	-0.01	0.45
Hospital LOS	-0.40	0.32	-1.25	0.22		
Patient factors						
Gender	-0.06	4.85	-0.01	0.99	0.37	0.00***
Prematurity	7.04	6.90	1.02	0.32		
Low birth weight	0.00	0.00	1.13	0.27		
Down syndrome	-24.30	5.49	-4.42	0.00***		
Growth (weight-for-age)	1.64	1.63	1.00	0.32		
Socio-demographic factors						
Distance service point	0.03	0.02	1.74	0.09	0.11	0.08
Age of mother	-1.03	0.39	-2.67	0.01*		
Maternal education	0.18	2.21	0.08	0.94		
Socioeconomic status	1.32	9.10	0.15	0.89		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.2: Variables predictive of BSID-III cognitive scores at three-months post cardiac intervention

BSID-III cognitive scores (3-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	4.03	2.24	0.00	1.00	-0.10	0.84
Type CHD	2.33	2.68	0.87	0.39		
Surgery an medical course						
Age at first surgery	-0.12	0.15	-0.82	0.43	0.04	0.37
CPB time	0.03	0.03	1.07	0.31		
Postop complications	-4.56	2.70	-1.69	0.12		
Duration of MV	5.83	3.57	1.63	0.13		
Hospital and ICU length of stay						
ICU LOS	0.44	0.35	1.25	0.23	-0.01	0.43
Hospital LOS	-0.11	-0.12	-0.89	0.38		
Patient factors						
Gender	0.47	1.10	0.42	0.68	0.45	0.00***
Prematurity	0.57	1.80	0.32	0.76		
Low birth weight	-0.00	0.00	-0.28	0.79		
Down syndrome	-6.20	1.30	-4.77	0.00***		
Growth (weight-for-age)	0.23	0.43	0.54	0.59		
Socio-demographic factors						
Distance service point	0.01	0.00	2.14	0.04*	0.28	0.03*
Age of mother	-0.22	0.07	-3.00	0.01**		
Maternal education	0.50	0.48	1.04	0.31		
Socioeconomic status	-0.14	2.25	-0.06	0.95		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.3: Variables predictive of BSID-III cognitive scores at six-months post cardiac intervention

BSID-III cognitive scores (6-months)	Estimates	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	-1.27	2.30	-0.55	0.59	0.01	0.37
Type CHD	3.77	2.74	1.36	0.19		
Surgery an medical course						
Age at first surgery	-0.14	0.16	-0.89	0.40	0.09	0.32
CPB time	0.02	0.02	1.49	0.17		
Postop complications	-5.20	2.58	-2.02	0.07		
Duration of MV	6.72	4.36	1.54	0.15		
Hospital and ICU length of stay						
ICU length of stay	0.35	0.28	1.23	0.24	-0.02	0.45
Hospital LOS	-0.13	0.21	-0.61	0.55		
Patient factors						
Gender	-0.67	1.15	-0.58	0.57	0.55	0.00***
Prematurity	0.87	2.14	0.40	0.69		
Low birth weight	0.00	0.00	0.46	0.65		
Down syndrome	-6.33	1.31	-4.83	0.00***		
Growth (weight-for-age)	0.56	0.44	1.29	0.21		
Socio-demographic factors						
Distance service point	0.01	0.00	1.51	0.15	0.26	0.06
Age of mother	-0.26	0.09	-3.00	0.01 **		
Maternal Education	0.42	0.53	0.80	0.44		
Socioeconomic status	-0.80	2.48	-0.32	0.75		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Disease type and severity were predictive of cognitive outcome only before cardiac intervention. Patient specific factors (especially the presence of DS) were predictive of cognitive outcome both before and after cardiac intervention. As a group of variables, socio-demographic factors were only predictive of cognitive outcome at three-month post cardiac intervention. However, maternal age as an individual variable was predicative of cognitive outcome both before and after cardiac

intervention. Distance to the cardiac service point as an individual variable was also found to be predictive of cognitive outcome at three-month post cardiac intervention.

Variables relating to the cardiac surgery and post-operative medical course as well as ICU and hospital length of stay were not predictive of cognitive outcome before or after cardiac intervention.

Language development

Table XIV.4: Variables predictive of BSID-III language scores at baseline

BSID-III language scores (baseline)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	-11.62	14.28	-0.81	0.42	0.02	0.37
Type CHD	-19.40	10.23	-1.90	0.07		
Surgery an medical course						
Age at first surgery	-1.46	0.44	-0.36	0.00**	0.30	0.02*
CPB time	-0.01	0.05	-0.29	0.77		
Postop complications	-2.92	7.34	-0.40	0.70		
Duration of MV	-6.67	9.73	-0.69	0.50		
Hospital and ICU length of stay						
ICU length of stay	-0.48	0.87	-0.55	0.59	-0.00	0.39
Hospital LOS	-0.04	0.26	-0.14	0.87		
Patient factors						
Gender	2.34	4.20	0.57	0.58	0.23	0.01**
Prematurity	5.88	5.98	0.98	0.33		
Low birth weight	7.88	3.82	0.02	0.98		
Down syndrome	-1.51	4.76	-3.18	0.00**		
Growth (weight-for-age))	2.72	1.42	1.93	0.06		
Socio-demographic factors						
Distance to service point	0.02	0.01	9.59	0.12	-0.01	0.48
Age of mother	-0.33	0.30	-1.10	0.28		
Maternal education	1.32	1.75	0.76	0.46		
Socioeconomic status	-3.00	7.21	-.0.41	0.68		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.5: Variables predictive of BSID-III language scores at three-months post cardiac intervention

BSID-III language scores (3-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	4.00	3.32	1.21	0.24	0.06	0.25
Type CHD	-1.00	3.96	-0.25	0.80		
Surgery an medical course						
Age at first surgery	-0.34	0.21	-1.62	0.13	0.20	0.16
CPB time	0.06	0.04	1.52	0.16		
Postop complications	-5.05	3.86	-1.31	0.22		
Duration of MV	-5.05	3.86	-1.31	0.22		
Hospital and ICU length of stay						
ICU length of stay	0.09	0.56	0.17	0.87	-0.02	0.46
Hospital LOS post-surgery	0.09	0.19	0.46	0.65		
Patient factors						
Gender	-0.79	1.94	-0.40	0.69	0.33	0.02*
Prematurity	0.23	3.17	0.07	0.94		
Low birth weight	0.00	0.00	0.22	0.83		
Genetic comorbidity (DS)	-7.68	2.30	-3.34	0.00**		
Growth (weight-for-age)	1.26	0.75	1.68	0.11		
Socio-demographic factors						
Distance to service point	0.01	0.01	1.56	0.13	-0.02	0.52
Age of mother	-0.15	0.14	-0.08	0.29		
Education of mother	0.31	0.92	0.34	0.74		
Socioeconomic status	-1.31	4.30	-0.30	0.76		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.6: Variables predictive of BSID-III language scores at six-months post cardiac intervention

BSID-III language scores (6-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	0.27	3.57	0.08	0.94	-0.14	0.92
Type CHD	2.93	4.24	0.69	0.50		
Surgery an medical course						
Age at first surgery	-0.40	0.24	-1.67	-0.13	-0.05	0.54
CPB time	-0.01	0.24	-0.30	0.77		
Postop complications	-1.16	4.0	-0.29	0.78		
Duration of MV	1.10	6.70	0.16	0.87		
Hospital and ICU length of stay						
ICU LOS	-0.08	0.42	-0.19	0.85	-0.07	0.72
Hospital LOS	-0.13	0.31	-0.42	0.68		
Patient factors						
Gender	1.31	5.86	0.22	0.83	0.29	0.74
Prematurity	1.10	8.07	0.14	0.90		
Low birth weight	0.00	0.00	0.63	0.54		
Down syndrome	-8.71	8.26	-1.06	0.31		
Growth (weight-for-age)	1.32	1.81	0.73	0.47		
Socio-demographic factors						
Distance service point	0.01	0.01	1.51	0.15	0.01	0.40
Age of mother	-0.21	0.14	-1.45	0.16		
Education of mother	0.54	0.88	0.61	0.55		
Socioeconomic status	-0.24	4.11	-0.06	0.95		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Variables relating to surgery and medical course (in particular age at surgery) were predictive of language performance before cardiac intervention. Patient specific factors (in particular the presence of DS) were predictive of language outcomes before cardiac intervention and at 3-months post cardiac intervention.

Disease severity and type, hospital and ICU length of stay, and sociodemographic variables were not found to be predictive of language outcomes.

Motor development

Table XIV.7: Variables predictive of BSID-III motor scores at baseline

BSID-II motor scores (Baseline)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	-21.50	18.60	-1.16	0.26	-0.09	0.88
Type CHD	-1.00	13.33	-0.08	0.94		
Surgery an medical course						
Age at first surgery	-0.50	0.67	0.75	0.46	-0.06	0.65
CPB time	0.05	0.07	0.70	0.49		
Postop complications	-14.27	11.25	-1.27	0.22		
Duration of MV	7.58	14.90	0.51	0.62		
Hospital and ICU length of stay						
ICU LOS	1.91	1.02	1.88	0.07	0.05	0.15
Hospital LOS	-0.59	0.30	-1.97	0.06		
Patient factors						
Gender	1.45	4.66	0.31	0.76	0.38	0.00***
Prematurity	4.90	6.63	0.74	0.47		
Low birth weight	-1.09	4.25	-0.03	0.98		
Down syndrome	-2.41	5.28	-4.57	0.00***		
Growth (weight-for-age)	3.27	1.63	-1.02	0.06		
Socio-demographic factors						
Distance to service point	0.01	0.02	0.41	0.69	0.05	0.22
Age of mother	-0.67	0.37	-1.83	0.07		
Education of mother	2.03	2.09	0.97	0.34		
Socioeconomic status	-9.24	8.64	-1.07	0.29		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.8: Variables predictive of BSID-III motor scores at three-months post cardiac intervention

BSID-III motor scores (3-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	p-value
Type and severity of CHD						
Disease severity	4.00	3.32	1.21	0.24	0.06	0.25
Type CHD	-1.00	3.96	-0.25	0.80		
Surgery an medical course						
Age at first surgery	-0.34	0.21	-1.62	0.13	0.20	0.16
CPB time	0.06	0.04	1.52	0.16		
Postop complications	-5.05	3.86	-1.31	0.22		
Duration of MV	6.18	5.10	1.21	0.25		
Hospital and ICU length of stay						
ICU LOS	0.09	0.56	0.17	0.87	-0.02	0.46
Hospital LOS	0.09	0.19	0.46	0.65		
Patient factors						
Gender	0.79	1.95	-0.41	0.69	0.33	0.02*
Prematurity	0.23	3.17	0.07	0.94		
Low birth weight	0.00	0.00	0.22	0.83		
Down syndrome	-7.67	2.30	-3.34	0.00**		
Growth (weight-for-age)	1.26	0.75	1.68	0.11		
Socio-demographic factors						
Distance service point	0.01	0.01	1.56	0.13	-0.03	0.52
Age of mother	-0.15	0.14	-1.08	0.29		
Education of mother	0.31	0.92	0.34	0.74		
Socioeconomic status	-1.31	4.30	-0.30	0.76		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.9: Variables predictive of BSID-III motor scores at three-months post cardiac intervention

BSID-III motor scores (6-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	P-value
Type and severity of CHD						
Disease severity	-2.53	4.81	-0.53	0.61	-0.02	0.49
Type CHD	7.80	5.72	1.36	0.19		
Surgery an medical course						
Age at first surgery	-0.08	0.35	-0.25	0.81	-0.05	0.53
CPB time	0.03	0.36	0.88	0.40		
Postop complications	-9.62	5.78	-1.67	0.13		
Duration of MV	14.89	9.78	1.52	0.16		
Hospital and ICU length of stay						
ICU LOS	0.75	0.57	1.31	0.21	-0.01	0.43
Hospital LOS	-0.34	0.43	0.79	0.44		
Patient factors						
Gender	-0.36	2.74	-0.13	0.90	0.39	0.02*
Prematurity	4.54	5.09	0.89	0.39		
Low birth weight	0.00	0.00	1.28	0.22		
Down syndrome	-11.61	3.11	-3.73	0.00**		
Growth (weight-for-age)	0.90	1.04	0.87	0.40		
Socio-demographic factors						
Distance service point	0.01	0.01	1.1	0.29	0.48	0.00***
Age of mother	-0.64	0.15	-4.41	0.00***		
Maternal education	1.17	0.90	1.30	0.21		
Socioeconomic status	-4.30	4.22	-1.02	0.32		

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Patient variables (in particular the presence of DS) were predictive of motor outcomes both before and after cardiac surgery. Socio-demographic variables (in particular maternal age) were found to be predictive of motor outcome at six-month post cardiac intervention.

Disease severity and type, surgery and medical course, hospital and ICU length of stay were not found to be predictive of motor outcomes.

VARIABLES PREDICTIVE OF HRQOL OUTCOMES

Table XIV.10: Variables predictive HRQOL scores at baseline

HRQOL total score (Baseline)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	P-value
Type and severity of CHD						
Disease severity	-15.04	12.08	-1.25	0.22	0.09	0.14
Type CHD	8.08	8.65	0.93	0.36		
Perioperative risk factors						
Age at first surgery	0.33	0.50	0.67	0.51	0.08	0.14
CPB time	0.09	0.05	1.72	0.10		
Patient factors						
Down syndrome	-1.49	4.68	-0.32	0.75	-0.00	0.43
Growth (weight-for-age)	-0.16	1.38	-0.12	0.91		
Feeding problems	7.31	4.67	1.56	0.13		
Socio-demographic factors						
Age of mother	-0.34	0.26	-1.31	0.20	-0.00	0.42
Maternal education	1.23	1.51	0.81	0.42		
Socioeconomic status	-2.99	6.31	-0.47	0.64		
Neurodevelopmental outcome						
Cognitive	0.01	0.14	0.12	0.91	0.17	0.02*
Language	-0.40	0.17	-2.37	0.02*		
Motor	0.40	0.15	2.73	0.01**		
Levels of parenting stress						
PSI-SF total score	-0.57	0.23	-2.49	0.01*	0.12	0.02*

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.11: Variables predictive HRQOL scores at three-months post cardiac intervention

HRQOL total score (3-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	P-value
Type and severity of CHD						
Disease severity	-3.14	15.15	-0.21	0.84	-0.10	0.83
Type CHD	7.58	18.11	0.42	0.68		
Perioperative risk factors						
Age at first surgery	-1.58	1.10	-1.44	0.17	0.07	0.24
CPB time	0.10	0.18	0.55	0.60		
Patient factors						
Down syndrome	-7.92	12.33	-0.64	0.53	-0.08	0.74
Growth (weight-for-age)	-2.51	3.50	-0.72	0.48		
Feeding problems	5.53	10.08	0.55	0.59		
Socio-demographic factors						
Age of mother	0.07	0.59	0.13	0.90	-0.07	0.70
Maternal education	4.26	3.90	1.09	0.29		
Socioeconomic status	-14.01	18.58	-0.75	0.46		
Neurodevelopmental outcome						
Cognitive	0.13	0.35	0.39	0.70	-0.12	0.95
Language	-0.24	0.47	-0.52	0.61		
Motor	0.08	0.39	0.20	0.84		
Levels of parenting stress						
PSI-SF total score	-0.92	0.50	-1.83	0.08	0.89	0.08

Indication of statistical significance: * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$

Table XIV.12: Variables predictive HRQOL scores at six-months post cardiac intervention

HRQOL total score (6-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R^2	P-value
Type and severity of CHD						
Disease severity	-2.77	15.40	-0.18	0.86	-0.17	0.95
Type CHD	9.96	25.05	0.40	0.70		
Perioperative risk factors						
Age at first surgery	-3.11	1.48	-2.11	0.06	1.19	0.16
CPB time	0.01	0.19	0.04	0.97		
Patient factors						
Down syndrome	-2.62	13.82	-0.19	0.85	-0.17	0.93
Growth (weight-for-age)	-1.21	3.86	-0.31	0.76		
Feeding problems	6.63	11.70	0.57	0.58		
Socio-demographic factors						
Age of mother	0.43	0.64	0.67	0.51	-0.06	0.59
Maternal education	5.07	4.28	1.19	0.25		
Socioeconomic status	-12.57	19.69	-0.64	0.53		
Neurodevelopmental outcome						
Cognitive	-0.09	42.7	-0.23	0.82	-0.13	0.83
Language	0.39	0.53	0.75	0.47		
Motor	0.04	0.44	0.09	0.93		
Levels of parenting stress						
PSI-SF total score	-0.02	0.58	-0.03	0.97	-0.06	0.97

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Neurodevelopmental outcome (in particular poor language and motor performance) and levels of parenting stress prior to cardiac intervention were predictive of parents having a poorer perception of their child's HRQOL.

Disease type and severity, perioperative factors, patient factors and socio-demographic factors were not predictive of HRQOL outcomes.

VARIABLES PREDICTIVE OF PARENTING STRESS OUTCOMES

Table XIV.13: Variables predictive parenting stress scores at baseline

PSI-SF total score (Baseline)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	P-value
Type and severity of CHD						
Disease severity	-5.35	8.52	-0.63	0.54	-0.04	0.64
Type CHD	1.60	6.10	0.26	0.80		
Perioperative risk factors						
Age at first surgery	-0.39	0.24	-1.65	0.11	0.04	0.11
Patient factors						
Down syndrome	-5.01	3.09	-1.62	0.11	-0.01	0.44
Growth (weight-for-age)	0.16	0.91	0.17	0.86		
Feeding problems	-0.81	3.08	-0.26	0.79		
Socio-demographic factors						
Age of mother	-0.10	0.18	-0.56	0.58	0.01	0.38
Maternal education	-1.50	1.00	-1.50	0.14		
Socioeconomic status	2.84	4.14	0.69	0.50		
Neurodevelopmental outcome						
Cognitive	-0.06	0.09	-0.65	0.52	0.07	0.13
Language	0.21	0.12	1.75	0.09		
Motor	0.07	0.10	0.68	0.50		
Perceived HRQOL						
PedsQL total score	-0.25	0.10	-2.49	0.01*	0.12	0.02*

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.14: Variables predictive parenting stress scores at three-months post cardiac intervention

PSI-SF total score (3-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	P-value
Type and severity of CHD						
Disease severity	3.83	5.85	0.66	0.52	-0.09	0.80
Type CHD	5.83	7.00	0.84	0.41		
Perioperative risk factors						
Age at first surgery	-0.66	0.30	-2.23	0.03*	0.14	0.03*
Patient factors						
Down syndrome	3.87	4.69	0.82	0.42	-0.04	0.57
Growth (weight-for-age)	1.51	1.33	1.13	0.27		
Feeding problems	-1.55	3.83	-0.40	0.69		
Socio-demographic factors						
Age of mother	0.39	0.21	1.86	0.08	0.15	0.12
Maternal education	-2.59	1.37	-1.89	0.07		
Socioeconomic status	10.45	6.39	1.64	0.11		
Neurodevelopmental outcome						
Cognitive	-0.07	0.12	-0.69	0.50	0.15	0.09
Language	0.42	0.16	2.66	0.01*		
Motor	-0.17	0.13	-1.29	0.21		
Perceived HRQOL						
PedsQL total score	-0.14	0.08	-1.83	0.08	0.09	0.08

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Table XIV.15: Variables predictive parenting stress scores at six-months post cardiac intervention

PSI-SF total score (6-months)	Estimate	Standard error	t-value	P>| t |	Adjusted R-squared	P-value
Type and severity of CHD						
Disease severity	-0.60	5.80	-0.10	0.92	-0.09	0.73
Type CHD	-0.93	6.91	-0.14	0.89		
Perioperative factors						
Age at first surgery	-0.26	0.32	-0.81	0.43	-0.02	0.43
Patient factors						
Down syndrome	2.25	4.72	0.48	0.64	-0.08	0.70
Growth (weight-for-age)	-0.99	1.39	-0.71	0.49		
Feeding problems	4.30	4.33	0.99	0.33		
Socio-demographic factors						
Age of mother	0.29	0.22	1.30	0.21	0.11	0.20
Maternal education	-2.65	1.39	-1.91	0.07		
Socioeconomic status	-0.00	0.01	-0.09	0.93		
Neurodevelopmental outcome						
Cognitive	-0.19	0.14	-1.37	0.19	-0.02	0.49
Language	-0.03	0.15	-0.21	0.84		
Motor	0.20	0.15	1.36	0.19		
Perceived HRQOL						
PedsQL total score	-0.00	0.10	-0.03	0.97	-0.06	0.97

Indication of statistical significance: * P < 0.05, ** P < 0.01 and *** P < 0.001

Parent's perception of their child's HRQOL was predictive of parenting stress prior to cardiac intervention. Age at first cardiac surgery and language performance, as individual variables were predictive of parenting stress at three-month post cardiac intervention.

Disease type and severity, patient-specific factors and socio-demographic factors were shown not to be predictive of parenting stress.

APPENDIX XV

OUTCOMES FOR CHILDREN WITH CONGENITAL HEART DISEASE AND DOWN SYNDROME

APPENDIX XV

OUTCOMES FOR CHILDREN WITH CONGENITAL HEART DISEASE AND DOWN SYNDROME

Findings for between group differences of children in this study with CHD with DS compared with those with CHD without DS for all reported parameters are reported below.

Table XV.1 Key demographic information

Variable	CHD with DS (n=10)	CHD without DS (n=30)
Age child at baseline (months)		
Median	9.3 [3.3 – 20.3]	7.2 [1.4 20.9]
Mean and SD	10.3 (±5.3)	8.9 (± 5.5)
Gender of the child		
Male	2 (20%)	13 (43.3%)
Female	8 (80%)	17 (56.7%)
Gestational age (weeks)		
Median	38 [32 – 40]	38[31 – 41]
Mean and SD	37.5 (±2.2)	37.5 (±2.02)
Preterm (<37 weeks gestation)	1 (10%)	8 (26.7%)
Term	9 (31%)	22 (73.3%)
Birth weight (grams)		
Median	2950 [1640 – 3950]	2795 [1690 – 3920]
Mean and SD	2904 (±680.3)	2870.3 (± 594.8)
LBW (< 2500g)	3 (30%)	7 (23.3%)
NBW (2500-4000g)	7 (70%)	23 (76.7%)
Age of the mother (years)		
Median	37 [24 – 42]	27.5 [16 – 43]
Mean	35.7 (±6.1)	27.6 (± 7.7)

Table XV.2 Socioeconomic statuses of families

Variable	CHD with DS (n=10)	CHD without DS (n=30)
Mean of education of mothers	Grade 9-11	Grade 9-11
Mean education level of fathers	Grade 9-11	Grade 9-11
Mean socioeconomic status	Lower class	Lower class

Table XV.3 Cardiac diagnostic information

Variable	CHD with DS (n=10)	CHD without DS (n=30)
Type of CHD		
Acyanotic	7 (70%)	23 (76.7%)
Cyanotic	3 (30%)	7 (23.3%)
Severity of the cardiac disease		
Mild	0	1 (3.3%)
Moderate	9 (90%)	21 (70%)
Moderate to severe	1 (10%)	7 (23.3%)
Severe	0	1 (3.4%)
Mean severity across the group	Moderate	Moderate

Table XV.4 Surgical information and postoperative medical course

Variable	CHD with DS (n=10)	CHD without DS (n=28)
Age at first surgery (months)		
Median	9.3 [3.3 – 20.3]	7.2 [1.4 – 20.9]
Mean	10.2 (±5.3)	9.1 (±5.7)
< 12 months at first surgery	7 (70%)	19 (67.9%)
> 12 months at first surgery	3 (30%)	9 (32.1%)
Cardiopulmonary bypass used		
Yes	8 (80%)	18 (64.3%)
No	2 (20%)	10 (35.7%)
CPB time (min)		
Median CPB time (minutes)	100.0[58 – 182]	104.5[41 – 300]
Mean CPB time and SD	108.8 (±41.4)	113.1 (±60.9)
Cross-clamping of the aorta		
Yes	8 (80%)	19 (67.9%)
No	2 (20%)	9 (32.1%)
Aorta cross-clamp time (minutes)		
Median	75.0 [24 – 124]	76.0 [15 – 132]
Mean	75.3 (±32.7)	68.3 (±37.2)
Cardiothoracic ICU LOS (days)		
Median	5 [4 – 28]	6 [3 - 22]
Mean	7.3 (±7.3)	7.6 (±4.9)
CTU stay > 7 days	1 (10%)	11 (39.3%)
CTU stay <7 days	9 (90%)	17 (60.7%)
Hospital LOS post surgery (days)		
Median	9 [6 – 108]	9 [3 – 64]
Mean	18.6 (±31.5)	13.3 (±12.2)
Length of stay >14 days	1 (10%)	7 (25%)
Length of stay ≤14 days	9 (90%)	21 (75%)

Table XV.5 Growth outcomes for participants with CHD with DS compared to CHD without DS

Growth parameter	CHD with DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Weight-for-age z-score		
Median	-2.6	-2.6
Mean and SD	-2.3 (±1.6)	-2.6 (±1.5)
Height-or-age z-score		
Median	-0.9	-2.0
Mean and SD	-1.5 (±3.0)	-2.4 (±2.3)
Head circumference-for-age z-score		
Median	-1.7	-1.4
Mean and SD	-1.6 (±0.9)	-1.3 (±1.7)
Three-months post cardiac intervention	**(n=5)**	**(n=20)**
Weight-for-age z-score		
Median	-1.1	-2.2
Mean and SD	-1.1 (±2.6)	-2.0 (±1.4)
Height-for-age z-score		
Median	-1.1	-0.7
Mean and SD	-2.2 (±2.5)	-1.1 (±1.5)
Head circumference-for-age z-score		
Median	-0.9	-1.0
Mean and SD	-1.8 (±1.9)	-0.6 (±1.7)
Six-months post cardiac intervention	**(n=5)**	**(n=17)**
Weight-for-age z-score		
Median	-1.2	-1.7
Mean and SD	-0.9 (± 2.1)	-1.8 (±1.8)
Height-for-age z-score		
Median	-1.6	-1.5
Mean and SD	-2.1 (±1.4)	-1.7 (±1.7)
Head circumference for age z-score		
Median	-1.6	-1.5
Mean and SD	-2.1 (±1.4)	-1.7 (±1.7)

Table XV.6 Classification of growth status according to z-scores for participants with CHD with DS compared to CHD without DS

Variable	CHD with DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Malnutrition	6 (60%)	21 (70%)
Stunting	4 (40%)	14 (46.7%)
Microcephaly	2 (20%)	8 (26.7%)
Three-months post cardiac intervention	**(n=5)**	**(n=20)**
Malnutrition	2 (40%)	12 (60%)
Stunting	2 (40%)	7 (35%)
Microcephaly	2 (40%)	3 (15%)
Six-months post cardiac intervention	**(n=5)**	**(n=17)**
Malnutrition	1 (20%)	8 (47%)
Stunting	2 (40%)	6 (35.3%)
Microcephaly	1 (20%)	2 (11.8%)

* z-score<-2 indicated malnutrition, stunting and microcephaly

Table XV.7 Neurodevelopmental outcomes for BSID-III scores for the cognitive, language and motor sub-scales for participants with CHD with DS compared to CHD without DS

Variable	CHD with DS	CHD without DS
Baseline	**(n=10)**	**(n=30)**
Cognitive sub-scale		
Median	60 [55 – 90]	95 [55 – 130]
Mean and SD	65 (±10.5)	91.5 (±16.5)
Language sub-scale		
Median	75.5 [62 - 112]	94 [65 – 115]
Mean and SD	78.2 (±15.2)	94.5 (±11.3)
Motor sub-scale		
Median	58 [46 - 88]	86.5 [58 – 112]
Mean and SD	61 (±14.1)	85.7 (±13.8)
Three-months post cardiac intervention	**(n=5)**	**(n=20)**
Cognitive sub-scale		
Median	55 [55 – 70]	90 [55 -105]
Mean and SD	60 (±7.1)	90.8 (±12.7)
Language sub-scale		
Median	71 [50 – 83]	92.5 [71 – 112]
Mean and SD	69.2 (±12.1)	93.2 (±13.1)
Motor sub-scale		
Median	46 [46 -73]	91 [46 – 112]
Mean and SD	55 (±12.7)	89.3 (±14.7)
Six-months post cardiac intervention	**(n=5)**	**(n=17)**
Cognitive sub-scale		
Median	55 [55 – 65]	90 [55 -100]
Mean and SD	58 (±4.5)	90.9 (±13.3)
Language sub-scale		
Median	65 [57 – 79]	91 [65 – 109]
Mean and SD	66.2 (±6.9)	88.8 (±13.5)
Motor sub-scale		
Median	55 [49 – 70]	97 [49 -121]
Mean and SD	57.4 (±8.3)	92.3 (±18.9)

* score < 70 = delayed, 70-84 at risk and >85 normal

Table XV.8 Classification of developmental performance according to the BSID-III scores for cognitive, language and motor sub-scales for participants with CHD with DS compared to CHD without DS

Variable	Time point	CHD with DS	CHD without DS
Cognitive	**Baseline**	**(n=10)**	**(n=30)**
Average or above		1 (10%)	22 (73%)
At risk		3 (30%)	6 (20%)
Delayed		6 (60%)	2 (7%)
Language			
Average or above		2 (20%)	26 (86.7%)
At risk		4 (40%)	3 (10%)
Delayed		4 (40%)	1 (3.3%)
Motor			
Average or above		1 (10%)	18 (60%)
At risk		2 (20%)	8 (26.7%)
Delayed		7 (70%)	4 (13.3%)
Cognitive	**Three-month follow-up**	**(n=5)**	**(n=20)**
Average or above		0 (0%)	17 (85%)
At risk		1 (20%)	2 (10%)
Delayed		4 (80%)	1 (5%)
Language			
Average or above		0 (0%)	14 (70%)
At risk		3 (60%)	6 (30%)
Delayed		2 (40%)	0 (0%)
Motor			
Average or above		0 (0%)	15 (75%)
At risk		1 (20%)	3 (15%)
Delayed		4 (80%)	2 (10%)
Cognitive	**Six-month follow-up**	**(n=5)**	**(n=17)**
Average or above		0	14 (82.4%)
At risk		0	2 (11.8%)
Delayed		5 (100%)	1 (5.8%)
Language			
Average or above		0	9 (52.9%)
At risk		1 (20%)	6 (35.5%)
Delayed		4 (80%)	2 (11.7%)
Motor			
Average or above		0	12 (70.6%)
At risk		1 (20%)	3 (17.6%)
Delayed		4 (80%)	2 (11.8%)

* scores < 70 delayed development , 70-84 at risk of developmental delay and ≥ 85 normal

Table XV.9 Perceived HRQOL for participants with CHD with DS compared to CHD without DS

PedsQL® total score	CHD with DS	CHD without DS
Baseline		
Median (range)	77.5 [63.9 – 88.2]	81.3 [48.6 – 97.2]
Mean and SD	75.5 (±8.1)	78.4 (±13.6)
Three-months post cardiac intervention		
Median (range)	77.8 [29.2 – 93.3]	90.3 [64.4 – 100]
Mean and SD	69.7 (±29.8)	87.9 (±11.2)
Six-months post cardiac intervention		
Median (range)	76.1 [74.4 -79.4]	89.5 [52.2 – 100]
Mean and SD	76.5 (±2.1)	87.3 (±11.3)

Table XV.10 Levels of parenting stress for participants with CHD with DS compared to CHD without DS

Sub-scales of the PSI-SF Baseline	CHD with DS (n=10)	CHD without DS (n=30)
Parenting distress		
Median (range)	87.5 [35 – 99]	90 [10 – 99]
Mean and SD	74.4 (±24.9)	86.4 (±17.3)
Parent-child dysfunction		
Median (mean)	95 [40 – 99]	80 [40 – 99]
Mean and SD	86.7 (±19.2)	77.8 (±19.8)
Difficult child		
Median (range)	75 [25 – 95]	77.5 [1 – 99]
Mean and SD	73 (±20.8)	65.2 (±27.9)
Total stress		
Median (range)	92.5 [40 – 99]	90 [5 - 99]
Mean and SD	82.4 (±20.9)	84.3 (±18.9)

Sub-scales of the PSI-SF Three-months post cardiac intervention	CHD with DS (n=5)	CHD without DS (n=20)
Parenting distress		
Median (range)	80 [30 – 95]	75 [1 – 95]
Mean and SD	68 (±30.9)	62.8 (±32.9)
Parent-child dysfunction		
Median (range)	95 [85 - 99]	70 [5 – 99]
Mean and SD	(93.6 (±6.1)	67 (±27.9)
Difficult child		
Median (range)	75 [50 - 95]	52.5 [1 – 95]
Mean and SD	75 (±18.4)	47.1 (±26.9)
Total stress		
Median (range)	90 [60 - 99]	77.5 [1 – 99]
Mean and SD	84.6 (±16.9)	65.1 (±29.8)

Sub-scales of the PSI-SF	CHD with DS	CHD without DS
Six-months post cardiac intervention	**(n=5)**	**(n=17)**
Parenting distress		
Median (range)	65 [35 – 95]	65 [1 – 95]
Mean and SD	62 (±24.9)	56.5 (±34.3)
Parent-child dysfunction		
Median (range)	95 [80 – 99]	55 [5 – 95]
Mean and SD	91 (±7.3)	55.1 (±34.6)
Difficult child		
Median (range)	80 [35 – 99]	40 [1 – 90]
Mean and SD	(76.8 (±24.7)	39.1 (±34)
Total stress		
Median (range)	80 [55 – 99]	50 [1 – 95]
Mean and SD	81.8 (±17.3)	50.8 (±35.8)

Table XV.11 Classification of levels of parental stress for participants with CHD with DS compared to CHD without DS

Timeframe	Sub-scale	CHD with DS (n=10)	CHD without DS (n=30)
Baseline	**Parenting stress**		
	Clinically significant	5 (50%)	19 (63.3%)
	High	6 (60%)	25 (83.3%)
	Normal	4 (40%)	4 (13.3%)
	Low	0 (0%)	1 (3.4%)
	Parent-child dysfunction		
	Clinically significant	8 (80%)	14 (46.7%)
	High	8 (80%)	14 (46.7%)
	Normal	2 (20%)	16 (53.3%)
	Low	0 (0%)	0 (0%)
	Difficult child		
	Clinically significant	3 (30%)	4 (13.3%)
	High	4 (40%)	10 (33.3%)
	Normal	6 (60%)	18 (60%)
	Low	0 (0%)	2 (6.7%)
	Total stress		
	Clinically significant	7 (70%)	17 (56.7%)
	High	7 (70%)	20 (66.7%)
	Normal	3 (30%)	9 (30%)
	Low	0 (0%)	1 (3.4%)

* >90th percentile clinically significant, >85th percentile high, 15th to 80 percentile low and <15th percentile low

Timeframe	Sub-scale	CHD with DS (n=5)	CHD without DS (n=20)
Three-months post cardiac intervention	**Parenting stress**		
	Clinically significant	2 (40%)	5 (25%)
	High	2 (40%)	9 (45%)
	Normal	3 (60%)	8 (40%)
	Low	0 (0%)	3 (15%)
	Parent-child dysfunction		
	Clinically significant	4 (80%)	7 (35%)
	High	5 (100%)	8 (40%)
	Normal	0 (0%)	11 (55%)
	Low	0 (0%)	1 (5%)
	Difficult child		
	Clinically significant	2 (40%)	1 (5%)
	High	2 (40%)	2 (10%)
	Normal	3 (60%)	16 (80%)
	Low	0 (0%)	2 (10%)
	Total stress		
	Clinically significant	3 (60%)	3 (15%)
	High	3 (60%)	6 (30%)
	Normal	2 (40%)	12 (60%)
	Low	0 (0%)	2 (10%)

* >90th percentile clinically significant, >85th percentile high, 15th to 80 percentile low and <15th percentile low

Timeframe	Sub-scale	CHD with DS (n=5)	CHD without DS (n=17)
Six-months post cardiac intervention	**Parenting stress**		
	Clinically significant	1 (20%)	4 (23.5%)
	High	1 (20%)	6 (35.5%)
	Normal	4 (80%)	8 (47.1%)
	Low	0 (0%)	3 (17.6%)
	Parent-child dysfunction		
	Clinically significant	4 (80%)	5 (29.4%)
	High	4 (80%)	5 (29.4%)
	Normal	1 (20%)	9 (52.9%)
	Low	0 (0%)	3 (17.6%)
	Difficult child		
	Clinically significant	2 (40%)	1 (5.9%)
	High	2 (40%)	3 (17.6%)
	Normal	3 (60%)	8 (47.1%)
	Low	0 (0%)	6 (35.3%)
	Total stress		
	Clinically significant	2 (40%)	5 (29.4%)
	High	2 (40%)	5 (29.4%)
	Normal	3 (60%)	8 (47.1%)
	Low	0 (0%)	4 (23.5%)

* >90th percentile clinically significant, >85th percentile high, 15th to 80 percentile low and <15th percentile low

APPENDIX XVI

OUTCOMES FOR CHILDREN WITH CYANOTIC HEART DEFECTS

APPENDIX XVI

OUTCOMES FOR CHILDREN WITH CYANOTIC HEART DEFECTS

Findings for between group differences for children with cyanotic compared with acyanotic heart defects for all parameters is reported below. Values reported are frequencies with percentages, medians with ranges and means with standard deviations.

Table XVI.1 Key demographic information

Variable	Cyanotic (n=8)	Acyanotic (n=32)
Age child at baseline (months)		
Median (range)	6.1 [3.3 – 20.9]	7.7 [1.4 – 20.3]
Mean and SD	8.4 (± 6.4)	9.4 (± 5.2)
Gender of the child		
Male	2 (25%)	13 (40.6%)
Female	6 (75%)	19 (59.4%)
Gestational age (weeks)		
Median (range)	38 [32 – 41]	38 [31 -40]
Mean and SD	38.1 (±2.7)	37.3 (±1.8)
Preterm (<37 weeks gestation)	1 (12.5%)	8 (25%)
Term	7 (87.5%)	24 (75%)
Birth weight (grams)		
Median (range)	2684.5 [2085 – 3920]	2975 [1640 – 3950]
Mean and SD	2825.5 (±707.4)	2892.2 (±593)
LBW (< 2500g)	3 (37.5%)	7 (21.9%)
NBW (2500-4000g)	5 (62.5%)	25 (78.1%)
Age of the mother (years)		
Median (range)	26.5 [19 – 43]	30 [16 – 42]
Mean and SD	28.9 (±10.30)	29.8 (±7.6)

Table XVI.2 Socioeconomic status of families

Variable	Cyanotic (n=8)	Acyanotic (n=32)
Mean of education of mothers	Grade 9-11	Grade 9-11
Mean education level of fathers	Grade 9-11	Grade 9-11
Mean socioeconomic status	Low class	Low class

Table XIV.3 Cardiac diagnostic information

Variable	Cyanotic (n=10)	Acyanotic (n=32)
Severity of the cardiac disease		
Mild	0 (0%)	1 (3.1%)
Moderate	1 (12.5%)	29 (90.6%)
Moderate to severe	6 (75%)	2 (6.3%)
Severe	1(12.5%)	0 (0%)
Mean severity across the group	Moderate to severe	Moderate

Table XVI.4 Surgical information and postoperative medical course

Variable	Cyanotic (n=8)	Acyanotic (n=30)
Age at first surgery (months)		
Median (range)	6.1 [3.3 – 20.9]	8.1 [1.4 – 20.5]
Mean and SD	8.5 (±6.4)	9.6 (±5.4)
< 12 months at first surgery	6 (75%)	20 (66.7%)
> 12 months at first surgery	2 (25%)	10 (33.3%)
Cardiopulmonary bypass used		
Yes	3 (37.5%)	23 (76.7%)
No	5 (62.5%)	7 (23.3%)
CPB time (minutes)		
Median (range)	134 [58 – 300]	104 [41-190]
Mean and SD	164 (± 123.8)	105 (±40)
Cross-clamping of the aorta		
Yes	3 (37.5%)	24 (80%)
No	5 (62.5%)	6 (20%)
Aorta cross-clamp time (minutes)		
Median (range)	74 [19 - 100]	76 [15 – 132]
Mean and SD	64.3 (±41.4)	71.1 (±35.6)
Cardiothoracic ICU LOS (days)		
Median (range)	7.5 [4 – 22]	5 [3 -28]
Mean and SD	9.8 (±6)	7 (±5.4)
CTU stay > 7 days	7 (87.5%)	8 (26.7%)
CTU stay ≤7 days	1 (12.5%)	22 (73.3%)
Hospital LOS post-surgery (days)		
Median (range)	14 [6 – 33]	8.5 [3 - 108]
Mean and SD	16.8 (±9.7)	14.1 (±20.7)
Length of stay >14 days	4 (50%)	4 (13.3%)
Length of stay ≤14 days	4 (50%)	26 (86.7%)

Table XVI.5 Growth outcomes for participants with cyanotic compared to acyanotic heart defects

Growth parameter	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Weight for age z-score		
Median	-2.8	-2.6
Mean and SD	-2.5 (±1.4)	-2.5 (±1.5)
Height for age z-score		
Median	-2.5	-1.6
Mean and SD	-3.3 (±2.8)	-1.9 (±2.3)
Head circumference for age z-score		
Median	-1.4	-1.4
Mean and SD	-1.5 (±2.2)	-1.3 (±1.4)
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Weight for age z-score		
Median	-2.9	-1.7
Mean and SD	-3.0 (±0.8)	-1.6 (±1.7)
Height for age z-score		
Median	-1.0	-1.2
Mean and SD	-1.2 (±1.6)	-1.6 (±1.9)
Head circumference for age z-score		
Median	0.3	-1.2
Mean and SD	0.2 (±1.7)	-1.1 (±1.7)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Weight for age z-score		
Median	-2.2	-1.8
Mean and SD	-1.8 (±2.5)	-1.6 (±1.7)
Height for age z-score		
Median	-1.8	-1.6
Mean and SD	-1.7 (±1.8)	-1.8 (±1.6)
Head circumference for age z-score		
Median	0.3	-0.6
Mean and SD	0.5 (±1.3)	-0.5 (±1.9)

Table XVI.6 Classification of growth status according to z-scores participants with cyanotic compared to acyanotic heart defects

Variable	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Malnutrition	6 (75%)	21 (65.6%)
Stunting	5 (62.5%)	13 (40.6%)
Microcephaly	2 (25%)	8 (25%)
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Malnutrition	4 (100%)	10 (47.6%)
Stunting	1 (25%)	8 (38.1%)
Microcephaly	0 (0%)	5 (23.8%)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Malnutrition	2 (50%)	7 (38.9%)
Stunting	2 (50%)	6 (33.3%)
Microcephaly	0 (0%)	3 (16.7%)

* z-score<-2 indicated malnutrition, stunting and microcephaly

Table XVI.7 Neurodevelopmental outcomes for BSID-III scores for cognitive, language and motor sub-scales for participants with cyanotic compared to acyanotic heart defects

Variable	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Cognitive sub-scale		
Median (range)	92.5 [55 – 105]	85 [55 – 130]
Mean and SD	89.4 (±17)	83.8 (±19.6)
Language sub-scale		
Median (range)	100 [65 – 112]	91 [62 – 115]
Mean and SD	93.9 (±17.5)	89.6 (±13.3)
Motor sub-scale		
Median (range)	85 [46 – 112]	82 [49 – 110]
Mean and SD	82.8 (±18.8)	78.7 (±17.3)
Three-month post cardiac intervention	**(n=4)**	**(n=21)**
Cognitive sub-scale		
Median (range)	90 [85 – 95]	90 [55 – 105]
Mean and SD	90 (±4.1)	83.6 (±18.5)
Language sub-scale		
Median (range)	106 [91 – 109]	83 [50 – 112]
Mean and SD	103 (±8.5)	85.6 (±15.7)
Motor sub-scale		
Median (range)	85 [82 – 94]	91 [46 – 112]
Mean and SD	86.5 (±5.7)	81.6 (±21.5)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Cognitive sub-scale		
Median (range)	95 [80 – 110]	87.5 [55 – 110]
Mean and SD	95 (±12.2)	80.8 (±18.7)
Language sub-scale		
Median (range)	90 [65 – 103]	81 [59- 109]
Mean and SD	87 (±17.9)	82.6 (±15.4)
Motor sub-scale		
Median (range)	89.5 [73 – 121]	89.5 [49 – 121]
Mean and SD	93.3 (±21.8)	82.3 (±22.8)

* score < 70 = delayed, 70-84 at risk and >85 normal, >85 normall

Table XVI.8 Classification of developmental performance according to the BSID-III for participants with cyanotic compared to acyanotic heart defects

Variable	Time point	Cyanotic	Acyanotic
Cognitive	**Baseline**	**(n=8)**	**(n=32)**
Average or above		6 (75%)	15 (46.9%)
At risk		1 (25%)	7 (21.8%)
Delayed		1 (25%)	10 (31.3%)
Language			
Average or above		6 (75%)	22 (68.8%)
At risk		0 (0%)	7 (21.9%)
Delayed		2 (25%)	3 (9.3%)
Motor			
Average or above		4 (50%)	15 (46.9%)
At risk		3 (37.5%)	7 (21.9%)
Delayed		1 (12.5%)	10 (31.3%)
Cognitive	**Three-month follow-up**	**(n=4)**	**(n=21)**
Average or above		4 (100%)	13 (61.9%)
At risk		0 (0%)	3 (14.3%)
Delayed		0 (0%)	5 (23.8%)
Language			
Average or above		4 (100%)	10 (47.6%)
At risk		0 (0%)	9 (42.9%)
Delayed		0 (0%)	2 (9.5%)
Motor			
Average or above		2 (50%)	13 (61.9%)
At risk		2 (50%)	2 (9.5%)
Delayed		0 (0%)	6 (28.6%)
Cognitive	**Six-month follow-up**	**(n=4)**	**(n=18)**
Average or above		3 (75%)	11 (61.1%)
At risk		1 (25%)	1 (5.6%)
Delayed		0 (0%)	6 (33.3%)
Language			
Average or above		2 (50%)	7 (38.9%)
At risk		1 (25%)	6 (33.3%)
Delayed		1 (25%)	5 (27.8%)
Motor			
Average or above		2 (50%)	10 (55.6%)
At risk		2 (50%)	2 (11.1%)
Delayed		0 (0%)	6 (33.3%)

* scores < 70 delayed development , 70-84 at risk of developmental delay and ≥ 85 normal

Table XVI.9 Perceived HRQOL for participants with cyanotic compared to acyanotic heart defects

PedsQL™ total score	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Median (range)	79.5 [48.6 – 93.3]	81 [49.3 – 97.2]
Mean and SD	75 (±16.2)	78.3 (±11.5)
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Median (range)	91.7 [88.9 – 99.3]	88.2 [29.9 – 100]
Mean and SD	92.9 (±4.6)	84.3 (±17)
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Median (range)	87.9 [84.8 – 90]	86.4 [52.2 – 100]
Mean and SD	87.6 (±2.3)	84.6 (±11.9)

Table XVI.10 Levels of parenting stress for participants with cyanotic compared to acyanotic heart defects

Sub-scales of the PSI-SF	Cyanotic	Acyanotic
Baseline	**(n=8)**	**(n=32)**
Total stress		
Median (range) Mean and SD	80 [50 -99] 78.5 (±19.1)	90 [5 – 99] 85.2 (±19.3)

Sub-scales of the PSI-SF	Cyanotic	Acyanotic
Three-months post cardiac intervention	**(n=4)**	**(n=21)**
Total stress		
Median (range) Mean and SD	75 [15-80] 61.3 (±31)	80 [1 – 99] 70.5 (±28.6)

Sub-scales of the PSI-SF	Cyanotic	Acyanotic
Six-months post cardiac intervention	**(n=4)**	**(n=18)**
Total stress		
Median (range) Mean and SD	25 [5 - 90] 36.3 (±37.1)	72.5 [1-99] 62.6 (±33.4)

Table XVI.11 Classification of levels of parental stress

Timeframe	Sub-scale	Cyanotic (n=8)	Acyanotic (n=32)
Baseline	**Total stress**		
	Clinically significant	3 (37.5%)	21 (65.6%)
	High	3 (37.5%)	24 (75%)
	Normal	5 (62.5%)	7 (21.9%)
	Low	0 (0%)	1 (3.1%)

Timeframe	Sub-scale	Cyanotic (n=4)	Acyanotic (n=21)
Three-month	**Total stress**		
	Clinically significant	0 (0%)	6 (28.6%)
	High	0 (0%)	9 (42.9%)
	Normal	4 (100%)	10 (47.6%)
	Low	0 (0%)	2 (9.5%)

Timeframe	Sub-scale	Cyanotic (n=4)	Acyanotic (n=18)
Six-month	**Total stress**		
	Clinically significant	1 (25%)	6 (33.3%)
	High	1 (25%)	6 (33.3%)
	Normal	2 (50%)	9 (50%)
	Low	1 (25%)	3 (16.7%

* >90th percentile clinically significant, >85th percentile high, 15th to 80 percentile low and <15th percentile low

APPENDIX XVII

HRQOL OUTCOMES ON THE PedsQL™ INFANT SCALES

APPENDIX XVII

HRQOL OUTCOMES ON THE PEDSQL™ INFANT SCALES

The HRQOL outcomes of children aged one to 12 months and 13 to 24 months respectively on the PedsQL™ Infant Scales are reported below. Values reported are medians with ranges and means with standard deviations

Table XVII.1 Perceived HRQOL of children aged one to 12 months on the PedsQL™ Infant Scales

Sub-scales	Baseline (n= 29)	Three-months post cardiac intervention (n= 15)	Six-months post cardiac intervention (n= 8)
Physical functioning			
Median (range)	88.3 [16.7-100]	100 [37.5 – 100]	100 [33 – 100]
Mean and SD	77 (±22.29)	89.9 (±31.46)	88.5 (±18.75)
Physical symptoms			
Median (range)	77.5 [35 – 95]	90 [45 – 100]	88.8 [50 – 100]
Mean and SD	75.5 (±15.73)	84.7 (±15.75)	84.6 (±13.21)
Emotional symptoms			
Median (range)	68.8 [16.7 – 100]	87.5 [25 – 100]	87.5 [62.5 – 100]
Mean and SD	68.4 (± 19.08)	80.6 (±15.75)	81.5 (±10.86)
Social functioning			
Median (range)	100 [50 -100]	100 [0 -100]	100 [62.5 – 100]
Mean and SD	95.7 (±11.58)	92.5 (±25.79)	94.3 (±11.5)
Cognitive functioning			
Median (range)	100 [37.5 – 100]	100 [25-100]	100 [25 – 100]
Mean and SD	90.7 (±18.19)	92.8 (±20.62)	83.7 (±23.36)
SUMMARY SCALES FOR THE PEDSQL® INFANT MODULES AS CALCULATED FROM THE ABOVE SUB-SCLAES			
Psychological health			
Median (range)	78.8 [48.8 – 100]	92.5 [20 – 100]	84.7 [59.6 – 100]
Mean and SD	78.3 (±12.85)	85.3 (±19.81)	83.4 (±11.67)
Physical health			
Median (range)	79.9 [29.7 – 95.8]	93.8 [42 – 100]	89.1 [42.1 – 100]
Mean and SD	76.1 (±17.27)	86.4 (±17.22)	86 (±14.15)
Total HRQOL score			
Median (range)	80.6 [48.6 – 97.2]	90.3 [29.9 – 100]	87.9 [52.2 – 100]
Mean and SD	77.3 (±13.24)	86 (±17.89)	85.1 (±11.18)

Table XVII.2 Perceived HRQOL of children aged 13 months to 24 months on the PedsQL™ Infant Scales

Sub-scales	Baseline (n= 11)	Three-months post cardiac intervention (n= 9)	Six-months post cardiac intervention (n= 10)
Physical functioning			
Median (range) Mean and SD	75 [34 – 100] 75 (±19.85)	94.4 [79.2 – 100] 94 (± 7.34)	100 [33 – 100] 88.5 (±18.75)
Physical symptoms			
Median (range) Mean and SD	80 [45 – 100] 78.9 (±16.93)	90 [72.5 – 100] 89.2 (±9.10)	88.8 [50 – 100] 84.6 (±13.21)
Emotional symptoms			
Median (range) Mean and SD	79.2 [52.1 – 95.8] 77.3 (±12.62)	60.4 [43.8 – 100] 71.7 (±21.89)	87.5 [62.5 – 100] 81.5 (±10.86)
Social functioning			
Median (range) Mean and SD	100 [55 – 100] 92.3 (±14.72)	100 [55 -100] 88.3 (±18.71)	100 [62.5 – 100] 94.3 (±11.5)
Cognitive functioning			
Median (range) Mean and SD	77.8 [44 -100] 81.1 (±20.61)	88.9 [0 -100] 78.1 (±34.21)	100 [25 – 100] 83.7 (±23.36)
SUMMARY SCALES FOR THE PEDSQL® INFANT MODULES AS CALCULATED FROM THE ABOVE SUB-SCLAES			
Psychological health			
Median (range) Mean and SD	74 [58.8 -95.2] 78.3 (±11.76)	80.8 [45.2 – 100] 78.1 (±20.30)	84.7 [59.6 – 100] 83.4(±11.67)
Physical health			
Median (range) Mean and SD	78.1[53.9 – 97.4] 7.5 (±15.28)	90.8 [79.7 – 100] 91.5 (±6.35)	89.1 [42.1 – 100] 86 (±14.15)
Total HRQOL score			
Median (range) Mean and SD	78.3 [64.4 – 95.6] 78.5 (±10.57)	84.4 [63.9 - 100] 83.8 (±13.44)	87.9 [52.2 – 100] 85.1(±11.18)

APPENDIX XVIII

PARENT INFORMATION LETTER AND INFORMED CONSENT FORM: PHASE III

APPENDIX XVIII

PARENT INFORMATION LETTER AND INFORMED CONSENT FORM: PHASE III

NEURODEVELOPMENT, QUALITY OF LIFE AND BURDEN OF CARE OF YOUNG CHILDREN WHO HAVE UNDERGONE CARDIAC INTERVENTIONS IN CENTRAL SOUTH AFRICA:
SIX WEEK AND SIX MONTH POST CARDIAC INTERVENTION OUTCOMES

Dear parent(s)/caregiver

As you know my name is Robyn Smith and I am a physiotherapist. I am currently doing research as part of my Doctorate of Philosophy (PhD) studies at the University of the Witwatersrand (WITS). Research is simply the process by which one finds the answers to a question.

Background and motivation

It is well known that many children with congenital heart defects have developmental problems. Currently no set developmental stimulation programme exists aimed at specifically addressing the developmental needs of children with congenital heart defects. Such a programme is aimed at optimising a child's development over time ensuring he reaches his full potential.

Aim of the study

As parents/caregivers you are a vital stakeholder in the process of developing a suitable home- based, parent driven developmental stimulation programme that meets

your needs as you will be the one implementing this programme in conjunction with your physiotherapist.

Your participation in the first phase of the study assisted me in identifying typical developmental problems found in children with congenital heart disease in central South Africa. I have used this information to now develop a programme that I need your help in evaluating.

Format of the study

You have been selected from the group of parents/caregivers that took part in Phase I and Phase II completing the first part of the study, I would now like to invite you to assist me in evaluating the home-based developmental stimulation programme that I have developed.

After agreeing to participate in the group discussion I will provide you with a date and time for the scheduled group session, I will reminded you telephonically of the session three days beforehand. The group will be held in an office at the Paediatric Cardiology Department, Universitas Academic Hospital in Bloemfontein that you are familiar with.

At the session you will be orientated about procedures and you will be asked to sign a consent form agreeing to participate. You will be provided with a pencil and eraser. A sheet with a question asking about the aspects you would like to have included in a home programme and another question about considerations you would like to have taken into account regarding a home programme will be handed out to you. Each question will be provided with a list of options. I will ask you to rank the aspects that you find important in order of priority in the blank block provided next to the items. The most important item is to be allocated the highest score. Once this is done I will issue you with a copy of the home programme I have compiled for the various age-groups. You will again go through the items per age group programme and rank each of the items independently in order of priority/importance for each age group specific programme in the blank block provided next to the items. Again the most important item is to be allocated the highest score. After this has been completed, the session

will then be adjourned and a date and time for a follow-up session will be fixed. This will give me a chance to calculate and consolidate your responses into a programme that reflects entire group's priorities.

You will again be reminded of the scheduled group appointment telephonically three days beforehand. At the next session the re-prioritised programme will be presented to the group and discussed until consensus is reached by the entire group that the programme address everybody's needs.

Each group session will take approximately one hour. Additional sessions may be needed if we have difficulty in finding consensus.

Benefit of participating in the study

Your input into the home programme will be invaluable in ensuring a relevant programme that also addresses your needs as parents/caregivers.

It is hoped that following this study this programme will be piloted and potentially implements for all children attending the Paediatric Cardiology Department at Universitas Academic Hospital if shown to be effective.

Ethical considerations

This part of the study holds no anticipated risk to you.

Your participation in this study is voluntary, you may decline to participate or withdraw from this part of the study at any point without the risk of discrimination or penalty. Your child will continue to receive standard care irrespective of your participation.

You will not be remunerated for your participation in this part of the study, but the researcher will reimburse you for your travelling costs for visits directly related to your participation in this study. An amount of R150 per visit will be provided per visit for transport. No additional costs will be incurred due to your participation.

All information you and others provide in these group sessions will be treated confidential.

Complete confidentiality cannot however be guaranteed, as this information may be required to be disclosed if requested by a court of law or an ethics committee.

Feedback on study outcome

The results of the study can be requested from the researcher following the completion of the study.

Presentation and publication of research findings

The results of the study may be used in presentations at academic congresses or in print in the form in an accredited journal. In the above cases all data pertaining to participants will be presented in an anonymous manner and no individual will be identifiable.

Ethical inquiries

This protocol has been reviewed by two ethics committee. If you have any questions or concerns pertaining to the ethical aspects of the study you may contact the researcher or the secretariats of the following ethics committees:

Ethics Committee of the Faculty of Health Sciences, University of Free State
Office of secretariat 051-4052812
StraussHS@ufs.ac.za

Medical Human Research Ethics Committee, University of Witwatersrand
Office of secretariat 011-7171234
anisa.keshav@wits.ac.za

If you have any inquiries, questions or concerns the research can be contacted at the following numbers:

Robyn Smith
Lecturer /Physiotherapist
Department of Physiotherapy
University Free State

051- 4013303 (w)
082 925 9367 (cell)

Informed consent

I ....., have been informed about the study by the researcher Mrs. Robyn Smith. I ..... agree to participate in this study.

I am aware that my participation is voluntary, and that I can decline participation or withdraw at any point without the risk of penalty. I am aware that my child will continue to receive standard care irrespective of my participation.

I am aware that I will only receive compensation of R150 per visit for travelling costs for my visits directly relating to my participation in this part of the study. I agree to attend the sessions as scheduled by Ms. Smith.

I have been informed that the information discussed in the groups is confidential and that I may not report any of the discussions to persons outside the confines of the group.

I am aware that if I have any ethical concerns I may approach the researcher or the secretariat of the ethics committees. I am aware that I can request the results of the study upon its completion.

I am aware that the results of the study may be presented at academic congresses or in print in the form in an accredited peer reviewed journal.

I am aware that I will be provided with a copy of the information letter and the signed copy of the informed consent for personal reference.

Signature of the parent/caregiver _____

Name in print _____

Date _____

Signature of the researcher _____

Name in print _____

Date _____

Signature of a witness _____

Name in print _____

Date _____

Signature of a translator _____

(If applicable)

Name in print _____

Date _____

APPENDIX IXX

EXPERT PANEL INFORMATION LETTER AND INFORMED CONSENT INSTRUCTIONS:

PHASE III

APPENDIX IXX

EXPERT PANEL INFORMATION AND INFORMED CONSENT LETTER: PHASE III

TITLE OF THE RESEARCH STUDY

NEURODEVELOPMENT, QUALITY OF LIFE AND BURDEN OF CARE OF YOUNG CHILDREN WHO HAVE UNDERGONE CARDIAC INTERVENTIONS IN CENTRAL SOUTH AFRICA:
THREE-MONTH AND SIX-MONTH POST CARDIAC INTERVENTION OUTCOMES

Dear Madam,

My name is Robyn Smith and I am a physiotherapist employed at the University of the Free State. I am currently doing research as part of my Doctorate of Philosophy (PhD) studies at the University of the Witwatersrand (WITS).

Background and motivation

Congenital heart defects (CHD) are the most common type of congenital defects. Approximately 1% of children are born with a heart defect. It is a serious health condition, and in more severe cases the defect can hold the risk of associated problems including impaired growth, delayed development and more serious neurological consequences such as cerebral palsy.

As a result of recent advances in the diagnosis, treatment and post-operative care, most heart defects can be successfully corrected during infancy. Today up to 85 % of children born with CHD, who receive the appropriate medical and/or surgical treatment survive. CHD is now viewed as a chronic health condition.

Increased survival has necessitated a shift away from simply looking at survival as a measure of outcome. There is a move toward considering longer-term outcomes and associated morbidity, these measures include functionally ability or developmental status, health-related quality of life and the extent of the continued burden of care place on families.

To date very little research regarding cardiovascular disease in children has been done in South Africa, resulting in a significant gap in information regarding the pre- and post-cardiac intervention outcomes of young children living with CHD.

We do know that children with CHD living in South Africa have a vastly different prognosis regarding morbidity and mortality when compared to children in developed countries. Late diagnosis and delayed treatment of CHD continues to place a significant burden on the healthcare system of South Africa aside from the detrimental effects this has on the outcome of the child, and the continued burden of care placed on the family.

The implementation of early developmental intervention services such as physiotherapy, occupational therapy and speech therapy in the holistic management of the child with CHD has universally been poorly delineated. Currently developmental intervention and rehabilitation guidelines for this population remain vague with a paucity of appropriate, standardised and validated home-based, caregiver-driven developmental stimulation programmes aimed at optimising developmental outcome in children with CHD. Only two research studies have been conducted to date on the implementation of early developmental therapy in this population. Both studies have unanimously concluded that hospital-based services do not meet the needs of children living with CHD. Compliance with hospital-based therapy has been shown to be extremely poor. It has been strongly recommended that appropriate home-based, caregiver-driven developmental stimulation programmes would serve best to address the needs of CHD survivors and their families.

Based on the developmental outcomes of participants in Phase I and Phase III of the study a home-based, caregiver-driven developmental stimulation programme has been

developed. Standardised and validated developmental test items contained in the Bayley Scales of Infant and Toddler development III (BSID III) were used as the basis. Anecdotal information provided by parents upon exiting the study was also taken into consideration when developing the programme. The programme thus includes information on age appropriate skills that need to be achieved, identification of worrying signs and guidelines for activities, play and toys caregivers can use to enhance development.

As an experienced physiotherapist, occupational therapist or speech therapist working in early intervention services in South Africa I am in need of your input into this programme. I would therefore like to invite you to participate in this phase of the study.

By reviewing and providing feedback on the programme you are consenting to your participation in the study.

Aim of the study

The aim of this study has been threefold; Phase I and II has determined the pre-cardiac intervention, as well as the three month and six month post cardiac intervention developmental outcome, health-related quality of life and burden of care in young children with congenital heart disease in central South Africa.

The aim of this, **Phase III**, of the study has been determining the nature and extent of the developmental challenges faced CHD survivors in central South Africa, and the subsequent development of a home-based, caregiver driven developmental stimulation programme to meet the needs of these children and their families.

Format of the study

Phase III of the study involves the participation of selected parents, and an experienced rehabilitation professionals to review and provide input on the programme.

You participation in this phase of the study will involve reviewing, and providing feedback on the developmental stimulation programme that has been developed. This will require approximately **45 minutes** of your time.

The programme has been forwarded to you electronically. You are requested to note your comments and suggestions in writing on a hard copy if you wish, or electronically by making use of track changes on the document.

You will be given three (3) to review and submit the document. A reminder to submit your feedback will be sent to you electronically and via SMS one (1) week before the submission deadline. You feedback can be submitted electronically, or in hard copy form for written changes. You are welcome to contact the researcher should you have any questions.

The researcher will consolidate the feedback provided by the rehabilitation professionals and the caregivers. The programme will be revised as needed and a revised copy will be forwarded to you for any final comments before the programme is finalised.

Value in the study

The development of a validated home-based caregiver driven developmental stimulation programme will serve to address the developmental needs of children living with CHD, their families and the therapists who serve them.

This programme will be piloted in the population going forward in further research projects.

Ethical considerations

There are no anticipated risks involved in your participation.

The study has been provided with ethical clearance from the University of the Free State (ECUFS 177/2013) and the University of the Witwatersrand (M131056).

Participation is voluntary, you may decline participation or withdraw from the study at any point without the risk of discrimination or penalty.

You will not be remunerated for your participation in the study. You may also not directly benefit from your participation.

All personal information will be treated as confidential, only the researcher will have access to this information. Complete confidentiality cannot however be guaranteed at this information may be required to be disclosed if requested by a court of law or by an ethics committee.

Feedback on study outcome

You may also request feedback following the conclusion of the study.

Presentation and publication of research findings

The results of this study may be used in presentations at academic congresses or in print in the form as a scientific article published in an accredited peer reviewed journals both locally and internationally. In the above cases all data pertaining to participants will be presented in an anonymous manner.

Ethical inquiries

If you have any questions or concerns pertaining to the ethical aspects of the study please feel free to contact the researcher or the secretariats of the respective Ethics Committees following submission of the protocol to the committees for review.

Ethics Committee of the Faculty of Health Sciences, University of Free State
Office of secretariat 051- 4052812
ethicsfhs@ufs.ac.za

Medical Human Research Ethics Committee, University of Witwatersrand
Office of secretariat 011-7171234
anisa.keshav@wits.ac.za

If you have any inquiries, questions or concerns the research can be contacted at the following numbers:

Robyn Smith
Lecturer /Physiotherapist
Department of Physiotherapy
University Free State

051- 4013303 (w)
082 925 9367 (cell)
051-4368311 (home)

Informed consent

By reviewing and providing feedback on the programme you are consenting to your participation in the study.

You aware that your participation is voluntary, and that you can withdraw at any point.

You are aware that you will not be compensated for your participation in this study. You hereby agree to review the programme and then submit the reviewed documents as requested by Ms. Smith within the stipulated timeframes.

You have been informed that the information that you provide will be treated as confidential.

You are aware that if you have any ethical concerns you may approach the researcher or the secretariat of the ethics committees. You are aware that you can request the results of the study upon its completion.

You are aware that the results of the study may be presented at academic congresses or in print in the form in an accredited peer reviewed journal.

THANK YOU FOR YOUR PARTICIPATION

APPENDIX XX

PARENT INFORMATION DOCUMENT ON CONGENITAL HEART DISEASE

APPENDIX XX

PARENT INFORMATION DOCUMENT ON CONGENITAL HEART DISEASE

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UNIVERSITY OF THE FREE STATE

DEPARTMENT OF CARDIOLOGY AND PHYSIOTHERAPY

CONGENITAL HEART DISEASE AND MY CHILD'S DEVELOPMENT:

WHAT PARENTS NEED TO KNOW

Department of Paediatric Cardiology, UFS©

UNIVERSITY OF THE FREE STATE

DEPARTMENT OF CARDIOLOGY AND PHYSIOTHERAPY

CONGENITAL HEART DISEASE AND MY CHILD'S DEVELOPMENT

What is congenital heart defect (CHD)?

Congenital heart defects (CHD) are the most common type of congenital birth abnormality found in children. One in every hundred children is born with a heart defect. A congenital heart defect is an abnormality or abnormalities in the formation of the rooms of the heart and/or the big blood vessels before birth.

How is a congenital heart defect treated?

Treatment will depend on how severe the heart defect is, and may require medication and/or cardiac procedures (catheterisation) and/or surgery.

Why are children with congenital heart defects at a higher risk of developmental difficulties?

CHD can cause changes in the blood flow to the brain before and after birth, this might affect the brain's development. In some cases low levels of oxygen in the blood and the fact that the heart is not working properly may result in your child being too tired to play and explore their surroundings. Often children with heart defects do not eat well and do not gain weight, leaving them without enough energy to play and explore.

Children who are admitted to hospital often or who spend long periods of time in hospital with chest infections or heart problems, may be at risk of developmental problems. Being in hospital is not the best environment for your child's development.

Children who have long hospital stays or other complications (premature birth, genetic or neurological conditions) are also at risk. Having heart surgery can also pose a risk to your child's development.

Not all children with heart defects, or those that have heart surgery will necessarily have delayed development.

Why is it important to stimulate my child's development?

It is very important for you to stimulate your child's development as much as possible both before and after heart surgery. The first three years of life are critical to your child's development. This is the period of time when the brain grows the fastest and they learn the most new things.

The most important factors in your child's development are eating well and growing, having a good home environment, providing them with the right care, having a loving caregiver and having the right type of stimulation. You as the caregiver have a big influence on your child's development, and by helping to provide the right type of stimulation at home you will help them reach their full developmental potential.

What are the right type of activities and stimulation I need to give my child?

Children develop certain skills at certain ages. Play is very important in young children for learning. It is important to make use of play- and daily activities such as dressing, feeding and bathing to encourage your child's development.

Through playing with your child and talking to them you will teach them to talk, explore their environment and learn new things. It is important that you do the right activities for your child's age and developmental level.

Refer to the activity tables for ideas on appropriate activities.

Why is it important to monitor my child's development at home?

It is important for you to monitor if your child is able to perform the activities and master the skills expected for their age.

This will include skills relating to:

- Speaking and understanding language.
- Thinking, learning and solving problems.
- Grasping and manipulation skills (hand function).
- Big muscle movements and physical activities such as sitting, crawling, standing and walking.

You will need to continue to monitor these activities and skills as your child grows, even if there are not any problems now. Problems with learning, concentration, schoolwork and behavior may only be noticed later on. Refer to the activity tables for the age appropriate skills your child should master. This will help you see if your child is not reaching the skills they are supposed to for their age.

Why is it important to monitor your child's weight and if they are growing?

It is important that you provide your child with good nutrition. Being well fed helps to provide the energy the brain needs to develop and for the muscle to get strong. Food also gives your baby energy to play and explore their surroundings. If your child is not growing well this could also have a negative effect on their development and prevent them from reaching the skills they should reach for their age. This is why it is important to have your child weighed regularly at the clinic and to monitor if they are gaining weight. If your child is not gaining weight talk to your local nursing sister. If there is a problem they will refer you to a doctor or dietician.

What should I do if I am worried about my child's development?

If your child is not reaching their age specific skills or is not gaining weight and growing it is worrying. You know your child best, so if you notice any worrying signs (see listed in the activity tables for his age group) or you are worried about your child's development talk to a healthcare worker as soon as possible (this could be a nurse, your doctor, a physiotherapist or an occupational therapist). If they think it is necessary they will refer you to a doctor, physiotherapist, occupational therapist, speech therapist, dietician or psychologist for further testing.

So what should I do if my child does have a developmental delay?

If a healthcare worker has identified a developmental delay it may be necessary for your child attend early intervention therapy services such as physiotherapy, occupational therapy or speech therapy at your nearest service point in order to help your child achieve their full developmental potential. Children do best if their developmental problems are addressed as soon as possible, but it is never too late to do something about it.

The therapists will provide you with advice, as well as an activity and exercise programme for you do at home daily. You might need to follow up with her on a regular basis to monitor your child's progress.

You can also do the activities as suggested in the activity tables to help your child in their development. Try and do these activities daily and incorporate them during activities such as play, dressing, bathing and feeding.

What if my child also has Down syndrome?

Down syndrome is a genetic abnormality, and 40 to 50% of children with Down syndrome also have heart defects.

Children with Down syndrome development slower than other children. Children with Down syndrome develop big muscle actions e.g. sitting, crawling and walking and other activities against gravity at a slower rate due to their low muscle tone (floppy), weak muscles and hypermobile joints. Children with Down syndrome also have delayed development of speech and language, thinking and problem solving skills as well as hand skills and grips.

Their heart defect therefore puts them at risk of making the developmental delay even worse for the reasons discussed in the sections above.

If your child has Down syndrome you should have your child referred to early intervention services (physiotherapy, occupational therapy and speech therapy) as soon as possible after birth at your nearest service point. Early intervention therapy

will be necessary to assist you in helping your child achieve and master developmental skills.

Remember when monitoring your child's developmental skills using the activity table below you will need to take into account their naturally slower rate of development by making use of the table at least one age group below his actual age. Look for the table which contains activities he can already do or start to do and work from there.

What precautions do I need to take after my child's heart operation?

Following your child's heart operation there will be some special instructions for caring for them. Please read the information below regarding limits on physical activity, wound care and general instructions.

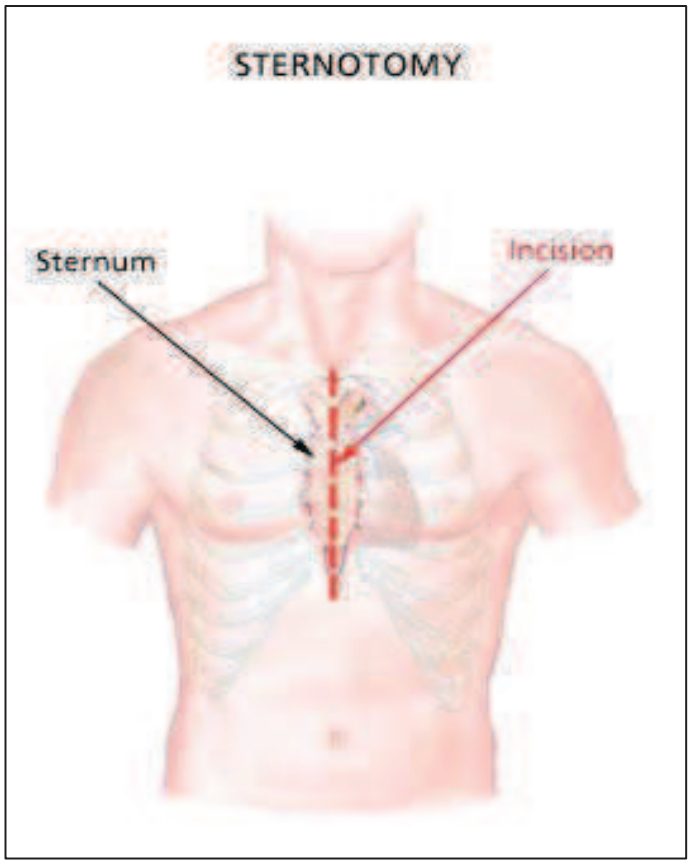

Image courtesy of GOOGLE images

PAEDIATRIC CARDIAC SURGERY DISCHARGE INSTRUCTIONS

Physical activity limitations for the first 6 weeks after surgery

Younger children (0 - 3 years)

Do not pick your child up by his/her arms or underneath their arms for at least 6 weeks. Rather pick your child up by scooping him/her up with one arm around the head, neck and shoulders and the other under the bottom.

Don't pull on your child's arms.

Try and avoid activities with the arms above the head, and try and avoid activities that require pushing with the arms or carrying heavy objects.

Put on clothing that buttons down the front rather than round necked tops that you need to pull over their head, this requiring you to lift their arms above their head to get into this can be painful and cause movement of the breastbone.

If your child has a cut through their sternum (breastbone) avoid putting them on their stomach for the first 4-6 weeks after the surgery as this is often very uncomfortable for your child. The breastbone heals in 6 weeks and from 6 weeks you should then again encourage "tummy time" during play with a goal of 30 minutes/day (this can be broken down into 4 sessions of 8-10 minutes each if your child does not like the position). Make sure your baby is breathing comfortably when you are putting them on their stomach.

Try and keep your child from crying for too long in the first weeks after surgery.

If you child is walking or is able to run try and avoid any activities that could cause your child to fall flat onto their chest. Also avoid activities that could cause your child to get a hard bump against their chest.

If your child is at an age where they are crawling it is difficult to prevent them from crawling. They will stop or avoid crawling if it is painful.

How much activity may my child do?

- For the most part it is difficult to limit children's levels of activity. They will rest when they are tired. It is however important in the period after the operation to watch them for signs of tiredness, and encourage them to rest when tired.
- It is normal for your child to rest and sleep more than usual in the weeks after the operation.

Return to day care or preschool

- If your child is attending day care or nursery school, you should discuss your child's return with your cardiologist or cardiothoracic surgeon before going home or at your first follow up visit. Your child will usually be allowed to return at 4-6 weeks after the operation. They may at first go back to school for half the day or only three days a week. Ask your doctor for clear instructions about this.

If my child has a developmental delay when can I start or restart early intervention services (physiotherapy, occupational therapy and speech therapy) after the surgery?

- It is important to give your child a chance to rest and recover after the surgery for at least 6 weeks.
- Therapy can be resumed after your 6 week follow-up at the cardiothoracic surgeon, but often children are only pain free from 3 months after the surgery when the sternum has healed completely. Discuss your child's return to therapy with your doctor and your therapists.
- Remember to inform your therapists that your child has had heart surgery recently as they may not always be aware.

Wound Care

- The wound can be left open to air once the nursing staff in the ward have taken of the dressing. Keep the wound dry and clean by following the wound care instructions given to you by the nursing staff.

- In smaller children the wound can be covered with a dry gauze dressing where there is moisture e.g. drooling or if they tend to spill drinking liquids onto the front of the chest. Immediately remove wet dressing and replace with a new dry dressing.
- Consider gauze dressing if the wound is being irritated by clothing or is itchy. Itching is a normal sign of healing.
- Protect the wound from the sun when it is still pink to decrease darkening of the scar. Keep the wound covered with clothing or a gauze dressing when your child is playing outside.
- Keep your child's nails short and do not let them scratch the wound or scar.
- DO NOT APPLY any creams or lotions to wound.
- Check the wound daily for any signs of infection e.g. redness, swelling, drainage from wound site or discomfort over the area (anything different than what you are used to seeing). This should be reported immediately to your local nursing sister or your doctor.
- Your child should only take a sponge bath (let the water run over the back) from the fifth day after surgery –try and keep the wound dry. Avoid bathing where the wound getting wet or being soaked until your doctor tells you otherwise.

General information

- Keep your child at home for the first few weeks after surgery and avoid crowded places like shopping malls to prevent exposure to germs.
- Wash your hands with soap and water before touching your child to avoid spreading any germs to your child.
- Postpone or delay scheduled immunizations until 6 weeks after the operation.
- Postpone or delay scheduled dentist appointments up until 3 months after the operation.
- Take the medication as instructed by your doctor- do not stop taking any medication or start a new medication before talking to your doctor. Make sure you attend your clinic visits to renew your medication prescriptions in time.

- It is essential that you attend your scheduled doctors and therapy appointments. If you cannot make an appointment please reschedule as soon as possible.

When should I take my child to the clinic or doctor?

- Running a fever.
- Has a very fast heartbeat.
- Is breathing very quickly or struggling to breathe.
- The wound looks infected (see above).
- Continuing nausea, vomiting and diarrhea.
- Poor feeding or if your child is not interested in eating.
- Discomfort or pain causing your child not to be comfortable or be able to sleep, and you feel your child is not getting better.
- Child is just lying and does not want to play.

Source documents

Brosig, Butcher, Ilardi, Sananes, Sanz, Sood, Struemph and Ware. Supporting development in children with heart disease. Cardiology patient page. *Circulation* 2014;130:e175-e176

Centers for Disease Control and Prevention (CDC). Milestone moments. Learn the signs. Act early.

Department of Education, South Africa and Unicef. Early learning and development ideas for parents and caregivers (images and information included may be freely abstracted and reproduced in part or in its whole)

Pearson. 20008. Bayley Scales of Infant and Toddler Development 3rd edition. Record booklet and administration manual.

Lucile Packard Children's hospital.2013. 3West Purple Team guidelines handbook. Patient discharge checklist pp 25-26

APPENDIX XXI

DEVELOPMENTAL ACTIVITY PROGRAMME

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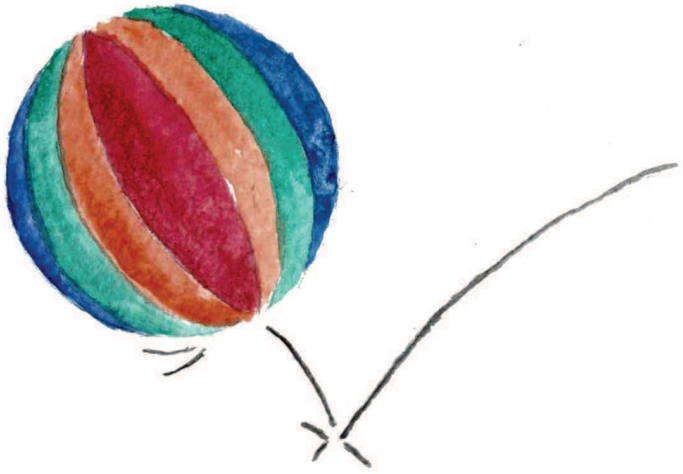
UNIVERSITY OF THE FREE STATE

DEPARTMENT OF CARDIOLOGY AND PHYSIOTHERAPY

DEVELOPMENTAL ACTIVITY PROGRAMME:

A GUIDELINE FOR PARENTS



Department of Paediatric Cardiology, University of the Free State ©

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DEVELOPMENTAL ACTIVITY SHEETS

How do I use the activity sheets below?

Please find tables below with activities your child should be doing for their age, worrying signs, and advice on activities you can do at home, and toys and items that are appropriate to play with.

Please note that if your child was born prematurely (before 37 weeks), and is still under the age of two years, you will need to subtract the weeks or months they were born early from their age to take into account for them being born early. This will ensure you measure your child development against the correct age expected skills.

Start with the activity sheet at your child's age (corrected age if born early). If they are unable to do the skills in this age group, work back one age group until you find an age group where they can do some of the skills or are starting to do some of the skills. Your child may not be on the same table for all the various skill areas e.g. physical activity, social and emotional and communication.

Illustrations by Rebecca Potterton

Department of Paediatric Cardiology, University of the Free State ©



ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS

0-3 MONTHS



WHAT BABIES SHOULD DO AT THIS AGE:

Physical development:

- When lying the baby moves arms and legs actively and the movements are smooth and rhythmical.
- When held upright over your shoulder baby can lift their head for a moment.
- When lying on their tummy baby can turn their head to both sides.
- Is able to watch your face or a toy with their eyes when it is moved in front of their face.
- Is able to bring both their hands to their mouth.



Learning, thinking and solving problems:

- Pays attention to faces and recognises you.
- Looks around.
- Turns their eyes and head towards the side of the sound when a rattle is or someone speaks loudly.

Language and communication:

- Smiles at the person speaking to them.
- Coos and makes gurgling sounds.



Department of Paediatric Cardiology, University of the Free State ©

Social and emotional skills

- Can calm themself by bringing their hands to their mouth.
- Will begin to smile.



You should be worried if your baby <u>does not</u>:

- Does not respond to loud noises.
- Does not bring hands to their mouth.
- Does not watch things as they move, or smile at you.
- Does not lift up their head when placed on their tummy, and dislikes the position.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist.

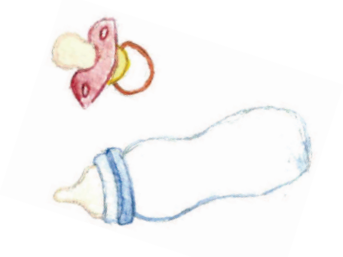
***

Things you can do to help your baby's development:

- Talk, read, sing and play with your baby during feeding, dressing, and bathing.
- Help your baby learn to calm herself. It's okay for them to suck on their hand and fingers to soothe themselves.
- Begin to help your baby get into a routine, such as sleeping at night more than in the day.
- Act excited and smile when your baby makes sounds. Copy your baby's sounds sometimes, but also talk normally to them using clear understandable language.
- Let baby practice watching a small toy by holding it up above their face and moving it up and down and to the left and right.
- It is important to hold your baby in an upright position over your shoulder allowing them to start lifting up their head off your shoulder. This will help to strengthen the neck muscles. Support the neck with your hand as needed.
- It is important to allow your baby to lie on their tummy when awake and during play, put toys nearby them when doing so. Encourage your baby to lift their head up when lying on their tummy by holding toys at eye level for them to look at.
- If your baby is not comfortable lying on its tummy on the floor you can let them lie on your chest while you lean back in a comfortable chair.
- It is best not to let your baby sleep on their stomach but rather on their back or side.

Toys and items you can use at home:

- Rattles (If you do not have a rattle use an empty pill container and fill with rice grains or maize pips- make sure container is sealed tightly).
- Hand held mirror for baby to look at themselves in (if you don't have a hand held mirror sit with your child in front of a large mirror).
- Bangle or plastic ring hung on a shoe lace or piece of string to encourage following with the eyes.
- Make sure toys do not have small loose parts which can be swallowed and cause your baby to choke.
- Make sure toys are small and light enough for baby to hold easily. Keep plastic toys clean by regularly washing them in warm water and dishwashing liquid.



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ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS

4-6 MONTHS



WHAT BABIES SHOULD DO AT THIS AGE:

Physical development:

- Can hold their head steady, without support when held in an upright position.
- Rolls from lying on their side back onto their back.
- Lying on their tummy, is able to push up on their arms and lift the head and upper body up off the ground.
- Sits with some support at the hips and back.

Learning, thinking and solving problems:

- Responds to the attention given by parent(s) or caregivers.
- Looks at their own hands.
- Explores objects by shaking them it or by putting them in their mouth.
- Approaches his/her image in a mirror with their body and/or touches the mirror.
- Always tries to reach for objects to get hold of them.



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Language and communication

- "Babbles" or makes baby noises.
- Cries in different ways when they are hungry, wet or tired.
- Put sounds together like "ah", "eh" and "oh".

Social and emotional skills:

- Knows familiar faces and may not like strangers.
- Clearly responds to sounds and voices.
- Responds to others emotions and is often happy.
- Like to look at themself in a mirror.



You should be worried if your baby <u>does not</u>:

- Does not try and get objects that are within reach.
- Does not to respond to the sounds around them.
- Does not show affection towards you.
- Cannot bring objects to their mouth to explore.
- Does not make sounds or respond to you.
- Does not roll over to the sides.
- Dislikes being placed on their tummy.
- Has difficulty calming down or getting into a routine.
- Does not smile or laugh.
- Feels very floppy or very stiff.
- Only uses one side of the body.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist.

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Things you can do to help your baby's development:

- Talk, read, sing and play with your baby during feeding, dressing, and bathing.
- Set a routine for sleeping and feeding.
- Act excited and smile when your baby makes sounds. Repeat your child's sounds and say simple words with those sounds. For example, if your child says "bah," say "baby" or "ball."
- Give age-appropriate toys to play with, such as rattle, ring or a small plastic blocks.
- Allow your baby to lie on a blanket on the floor, providing safe opportunities for your baby to play and reach for toys and explore their surroundings.
- Put toys near your baby so that she can reach for them. This will encourage them to start rolling.
- Put toys or rattles in your baby's hand and help him to hold them and pass them from one hand to the other.
- Hold your baby upright with feet on the floor as they will begin to "stand" with support.
- Place your baby on their tummy when awake and during play, put toys nearby them. This will encourage them to reach out for the toys.
- If your baby finds it hard to play while they are on their tummy, place a small rolled up towel under their chest.
- Use "reciprocal" play—when they smiles, you smile; when they makes sounds, you copy them.
- Read children's story books or picture books to your child every day. Praise them when they babble and "read" too.

Toys and items you can use at home:

- Rattles (if you do not have a rattle use an empty pill container and fill with rice grains or maize pips- make sure container is sealed tightly) or small toys that he/she is able to grasp easily and that are light.
- Small wooden or plastic blocks (if you do not have blocks use small empty match boxes).
- Hand held mirror or sit with your child in front of a large mirror.
- Bangle/plastic ring on a shoe lace or piece of string.
- A small ball e.g. a tennis ball
- Hard cover picture books (if you do not have a picture book you can use a magazine with bright pictures of familiar items. You can also cut pictures out of a magazine and paste in an exercise book to make your own picture book).



ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS



7 - 9 MONTHS

WHAT BABIES SHOULD DO AT THIS AGE:

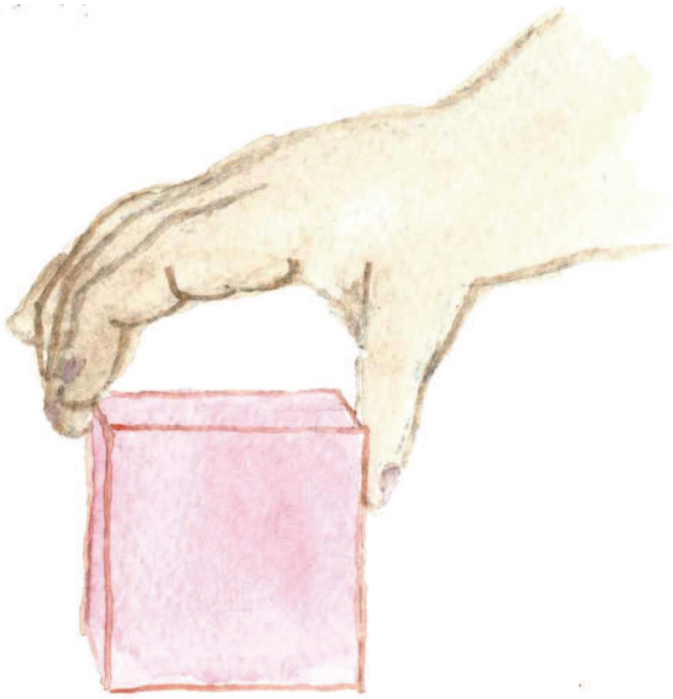
Physical development:

- Sits with slight support and later alone from around 8 months.
- Can roll from the back onto both sides, and later onto the tummy.
- Stands holding on to your hands or stands at a couch or low table.



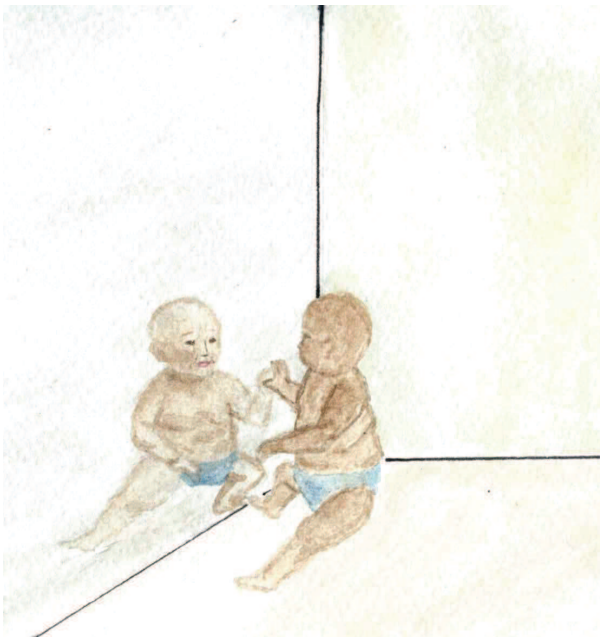


- Can move frcrylying onto their tummy and up into a crawling position.
- Starts to crawl.
- Picks up a block with one or both hands.
- Able to pick up a small object e.g. cereal “cheerios”.
- Can pass a plastic ring or block from one hand to the other.



Learning thinking and problem solving:

- Child plays with their image in a mirror (smiling, touching and mouthing).



- Plays with a string tied to a ring or bangle by pulling or chewing on the string.
- Bangs blocks, spoons during play.
- Looks for a fallen toy when dropped on floor.
- Reaches for toys all the time.

Language skills:

- Turns head towards the side of sounds.
- Recognises and turns head when their name is called.
- Makes sounds and tries use their voice to gain attention.

- Makes sounds like “gaga” “baba”, “dada”

Social and emotional skill:

- Responds to others emotions and is often happy.
- Like to look at themself in a mirror.
- Makes noises and laughs in response to speaker’s attention.

You should be worried if your baby <u>does not</u>:

- Does not take weight on their legs when you hold them in standing.
- Does not make sounds like “gaga”, “mama”, “dada” or “baba”.
- Does not sit alone or with very little help.
- Does not play games taking turns back and forth.
- Does not roll over to both sides and onto the stomach.
- Does not pass toys from one hand to the other, cannot pick up a small item.
- Seems very floppy or very stiff.
- If the muscles are weak.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist.

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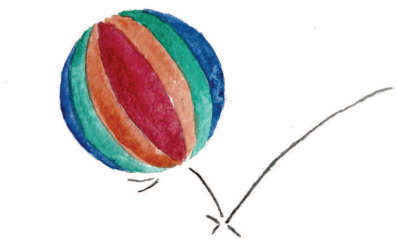


Things you can do to help your baby's development:

- Pay attention to the way they react to new situations and people; try to continue to do things that make your baby happy and comfortable. As they moves around more, stay close so they know that you are near.

- Describe what your baby is looking at; for example, "red, round ball." Copy your baby's sounds and words. But also talk to them using normal language.

- Ask for behaviours that you want e.g. "let's sit down" or "turn onto your tummy".

- Teach cause-and-effect by letting an object fall to the floor and help them look for it.

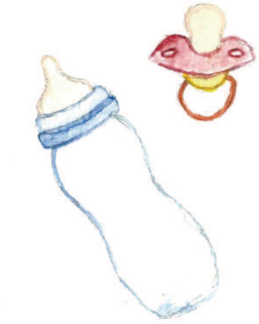
- Provide lots of room for your baby to move and explore in a safe area on the floor for example on the soft mat or on a blanket.

- Encourage play in sitting, give toys to your child from the front and sides to help develop sitting balance.

- When lying on their tummy put toys out in front of them just out of reach encouraging them to crawl forwards to get to the toy.

Toys and items you can use at home:

- Small plastic or wooden blocks (if you do not have blocks use a small empty match boxes).
- Kitchen spoons (metal or wooden) for banging.
- Cheerios' cereal to develop small hand skills.
- Plastic stack rings or bangle on a string or shoelace.
- Hand held mirror or sit with your baby in front of a large mirror.
- Hard cover picture books (if you do not have a picture book use a magazine with bright pictures and make a picture book).
- Plastic ball.



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ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS



10-12 MONTHS

WHAT BABIES SHOULD DO AT THIS AGE:

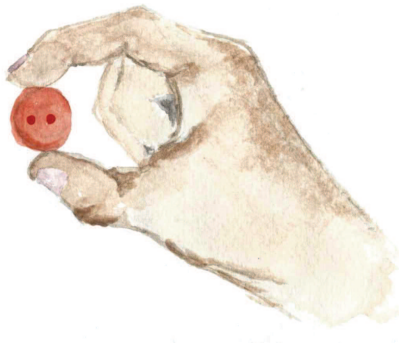
Physical development:

- Sits alone with good balance, and can turn and reach for toys put to the sides.
- When holding child under their arms in standing they step with their feet.
- Able to move around by crawling.
- Moves from lying to sitting or into a crawling position on their own.
- Stands against furniture for support.





- Able to pull themself up into standing from the ground against the furniture.
- Walks sideways along the furniture.
- Able to pick up a small object e.g. cereal “cheerios”” using thumb and first finger.
- Can pass ring or block from one hand to the other.
- Bangs spoons or blocks together or against surfaces.





Learning thinking and problem solving:



- Child will pick up two small blocks one in each hand.
- Will look at pictures with interest.
- Will pull on a string attached to a ring to bring it closer to grab.

Language skills:

- Turns head and stops playing when their name is called.
- Can start to identify different sounds.
- Tries to get your attention using their voice.
- Child will use gestures to indicate what they want e.g. point to something when



Social and emotional skills:

- Shy and nervous around strangers.
- Cries when mom, dad or a caregiver leaves them.
- Has favourite toys and people.Gets scared in some situations.
- Plays games e.g. hide and seek.

You should be worried if your baby <u>does not</u>:

Does not crawl.

- Cannot stand with support.

Does not search for things that fall.

- Does not point to things.
- Does not use gestures e.g. waving and pointing.
- Does not say any words.

Seems very floppy or very stiff.

- Loses skills that they had.

Struggling to learn to chew food.

- Difficulty seeing or hearing.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist.

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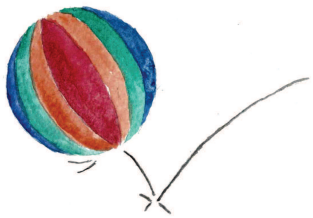


Things you can do to help your baby's development:

- Give your child time to get to know a new caregiver. Bring a favourite toy, stuffed animal, or blanket along to help comfort your child.
- In response to unwanted behaviours, say "no" firmly.
- Give your child lots of hugs, kisses, and praise for good behaviour. Encourage good behaviour.
- Talk to your child about what you're doing. For example, "mommy is washing your face with a cloth."
- Read to your child every day and tell them stories.
- Build on what your child says or tries to say, or what he points to. If he points to a truck and says "t" or "truck," say, "Yes, that's a big, blue truck."
- Play with blocks and other toys that encourage your child to use their hands. Offer them blocks by handing it to them one at a time (up to three blocks).
- Hide small toys and other objects under a facecloth and have your child find them.

Toys and items you can use at home:

- Small wooden or plastic blocks (if you do not have blocks use a small empty match boxes).
- Spoons (metal or wooden), pots and plastic containers.
- Cheerios' cereal rounds to develop fine grasp (safe as it dissolves if swallowed- avoid other small objects as they are choking hazards).
- Hard cover picture and story books (if you do not have a picture book use a magazine with bright pictures and make a picture book).
- Furniture such as low coffee tables, benches, chairs and couches to pull up against and walk alongside.
- Ball.





ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS



13 -18 MONTHS

WHAT BABIES SHOULD DO AT THIS AGE:

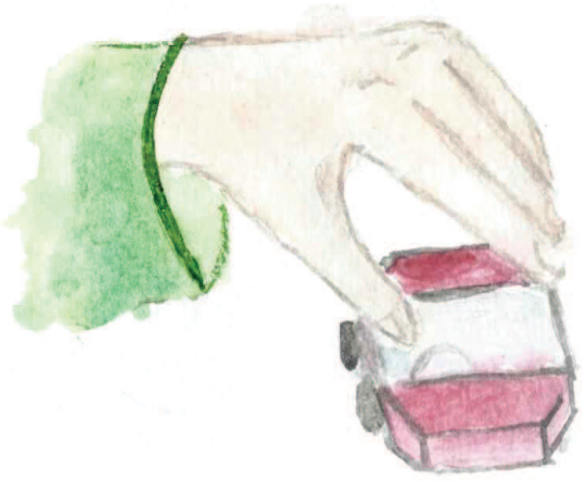


Physical development:

- Can sit down from a standing position.
- Can stand up alone from the ground.
- Can walk on their own (at least by 18 months).
- Can stand and throw a ball.
- Can turn pages in a book.
- Builds a two block tower.
- Starts to scribble on paper with a pencil or usually a crayon.

Learning thinking and problem solving:

- Looks for blocks in a cup/ container once they have been removed.
- Can take blocks out of cup/ container and back them back in.
- Can find a hidden toy under a face cloth.
- Child can turn a bottle/ jar upside down to get an item out of the bottle/ jar.
- Can push a car with all four wheels flat on the ground.



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Language skills:

- Child stops playing or what they are doing when you call his/her name.
- Makes sounds like “gaga” “baba”, “dada”.
- Uses sounds that sound like a word e.g. “mama”, “dada”.
- Points to objects you ask him to show you.
- Stops an activity when you say no-no.

Social and emotional skills:

- Likes handing objects to people as part of play.
- Can have temper tantrums.
- Scared of strangers.
- Show affection to familiar persons.
- Clings to parent when faced with new situations.

You should be worried if your baby <u>does not</u>:

- Does not point to things.
- Does not know what familiar things are.
- Very slow to walk and cannot yet walk.
- Does not notice or mind if parent leaves the room.
- Does start to say words.
- Difficulty sleeping.
- Difficulty eating solid food.
- Extreme fear of new people or situations.
- Loses skills that he/she had.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist

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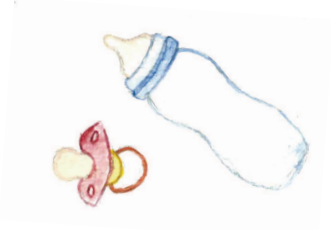


Things you can do to help your baby's development:

- At this age, children still play next to (not with) each other and don't share well. For play dates, give the children lots of toys to play with. Watch the children closely and step in if they fight or argue for a toy. They have not yet learnt to share.

- Give your child attention and praise when they follow instructions. Do not pay a lot of attention to bad behaviour. Spend a lot more time praising good behaviours than punishing bad ones.

- Do not scold your child when he says words incorrectly. Rather, say it correctly. For example, "That is a *ball*."

- Encourage your child to say a word instead of pointing. If your child can't say the whole word ("milk"), give her the first sound ("m") to help. Over time, you can encourage your child to say the whole sentence — "I want milk."

- Hide your child's toys around the room and let him find them.

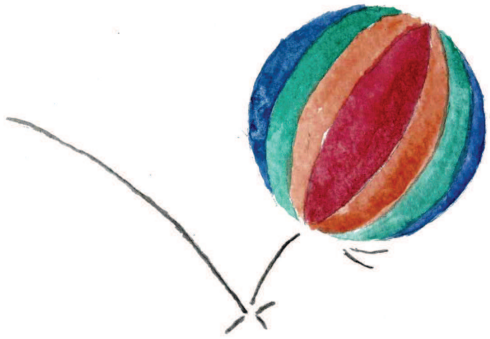
- Encourage your child to play with blocks. Take turns building towers and knocking them down.

- Do art projects with your child using crayons, paint, and paper. Describe what your child makes and hang it on

Toys and items you can use at home:

- Small blocks (if you do not have blocks use a small empty match boxes).
- Spoons (metal or wooden), plastic containers, pots and plastic containers.
- Cheerios' cereal rounds are a safe item to use to develop fine grasping skills (avoid other small items as they pose a choking hazard). Can pack them into a container/ jar and take them out.
- Cars and dolls.
- Hard cover picture books (if you do not have a picture book use a magazine with bright pictures and make a picture book).
- Paper and crayons or pencils.
- Everyday items e.g. plastic cup, spoons, facecloth and comb.

- Shape board with circle, square and triangle. If you do not have a shape board you can make your own out of a thick piece of cardboard from a shop box. Cut out a square board and copy the shapes included at the back of the document onto the cardboard. Cut out matching shapes from another piece of cardboard. To make picking the pieces up easier stick on a plastic coke bottle lid.





ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS



19 - 24 MONTH

WHAT BABIES SHOULD DO AT THIS AGE:

Physical development:

- Can bend down from a standing position to pick up a ball on the floor.
- Can climb up stairs using a hand rail, he/she puts both feet on a step before climbing up the next step.
- Can walk by themself and is stable on their feet.
- Can stand up alone, not holding onto anything.
- Can hold a crayon and scribbles on paper, grasps crayon with whole hand.
- Can build a two block tower.
- Can pack blocks into a container, and take them out again.





Learning thinking and problem solving:

- Able to find a completely hidden toy.
- Can unscrew lid from a container/ jar that is not tightly screwed on.
- Can play with spoon, cup, and facecloth using the items correctly.
- Can put at least one piece correctly in a shape board (square, circle, triangle).
- Can pack blocks into a container, and take them out again.

Language skills:

- Can respond to, and follow a simple spoken request e.g. come here.
- Identifies and names familiar items in their environment e.g. cup, ball, spoon.
- Identifies and names familiar pictures in a picture book or magazine.
- Understands concept like wait, my turn, and stop.
- Combines words and gestures e.g. by-bye with waving, want that with pointing.

Social and emotional skills:

- Copies adults and other children.
- Enjoys being with other children.
- Is more independent.
- Does what he has been told not to do.
- Plays beside other children rather than with them.



You should be worried if your baby <u>does not</u>:

- Does not know what to do with familiar things e.g. spoon.
- Does not follow up actions with words.
- Cannot walk steadily on their own.
- Cannot follow simple instructions.

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- Does not gain new words.
- Difficulty sleeping.
- Difficulty eating solid food.
- Extreme fear of new people or situations.
- Loses skills that they had.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist.

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Things you can do to help your baby's development:

- At this age, children still play next to (not with) each other and don't share well. For play dates, give the children lots of toys to play with. Watch the children closely and step in if they fight or argue.

- Give your child attention and praise when he follows instructions. Limit attention for defiant behaviour. Spend a lot more time praising good behaviours than punishing bad ones.

- Do not correct your child when he says words incorrectly. Rather, say it correctly. For example, "That is a *ball*."

- Encourage your child to say a word instead of pointing. If your child can't say the whole word ("milk"), give her the first sound ("m") to help. Over time, you can prompt your child to say the whole sentence — "I want milk."

- Hide your child's toys around the room and let him find them.

- Encourage your child to play with blocks. Take turns building towers and knocking them down, as well as activities packing blocks into plastic cup/ container and taking them out.

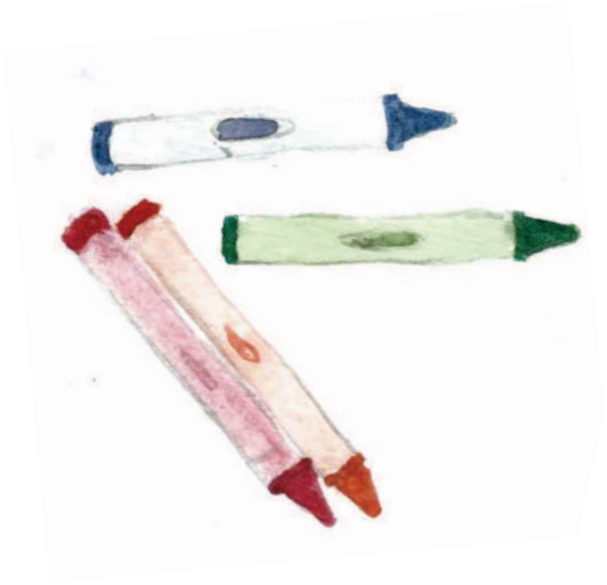
- Play games such as hide-and-seek and catches.

- Do art projects with your child using crayons, paint, and paper. Describe what your child makes and hang it on the wall or refrigerator.

Toys and items you can use at home:

- Small blocks (if you do not have blocks use a small empty match boxes).
- Cereal Cheerios' to practice fine grips- packing them into a container/ jar and taking them out.
- Cars and cars.
- Balls.
- Everyday items e.g. comb, face cloth, cup, spoon etc.
- Hard cover picture books (if you do not have a picture book use a magazine with bright pictures and make a picture book).
- Paper and crayons or pencils.

- Shape board with circle, square and triangle. If you do not have a shape board you can make your own out of a thick piece of cardboard from a shop box. Cut out a square board and copy the shapes included at the back of the document onto the cardboard. Cut out matching shapes from another piece of cardboard. To make picking the pieces up easier stick on a plastic coke bottle lid.





ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS



24 -36 MONTHS

WHAT BABIES SHOULD DO AT THIS AGE:



Physical development:

- Can bend down from a standing position to pick up a ball.
- Runs with good coordination.
- Can climb up- and down stairs using a hand rail.
- Can take steps backwards and to the sides.
- Can stand on one leg while holding on.
- Can hold a crayon and scribbles on paper.
- Can build a block tower with more than two blocks.
- Grasps crayon with thumb, index and middle finger (three finger grip).
- Starts to use one hand more than the other for activities.
- Can take connecting blocks (blocks that stick /fit together) apart.

Learning thinking and problem solving:

- Places all three shapes in shape board (circle, square and triangle).
- Can listen to a whole story in a book with attention.
- Can assemble a two piece puzzle.
- Can match pictures of the same thing.
- Can use item in an imaginary way e.g. a ball as an apple, a block as soap.

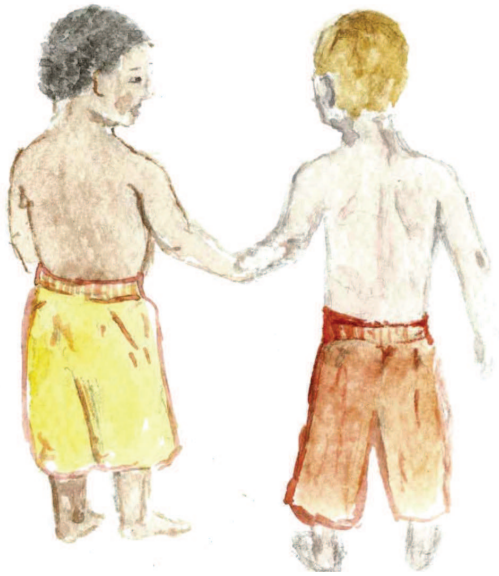
Language skills:

- Can follow instructions with two steps e.g. go and fetch the ball and bring it here.
- Identifies and names familiar items in the environment.
- Identifies clothing items e.g. shoes, shirt, hat, socks.

- Identifies action pictures e.g. sleeping, eating, playing, and driving a car.
- Knows what objects are used for.
- Uses at least eight words correctly.
- Can answer “yes” and “no”.
- Uses two word sentences e.g. mommy ball.

Social and emotional skills:

- Copies adults and other children.
- Shows affection towards friends.



You should be worried if your baby <u>does not</u>:

- Does not know what to do with familiar things e.g. spoon.
- Does not follow up actions with words and has trouble understanding.
- Cannot walk steadily and climb stairs holding on.
- Cannot follow simple instructions.
- Does not gain new words or speak clearly .
- Poor coordination
- Extreme and frequent tantrums.
- Loses skills that he/she had.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist.

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Things you can do to help your baby's development:

- Go to play groups with your child or other places where there are other children, to encourage getting along with other children.

- Set rules and limits for your child, and stick to them. If your child breaks a rule, give him a time out for 30 seconds to 1 minute in a chair or in his room. Praise your child for following the rules.

- Give your child instructions with two or three steps e.g. "Go to your room and get your shoes and hat."

- Read to your child every day. Ask your child to point to things in pictures and ask them to repeat words after you. Also ask them to identify objects.

- Give your child an "activity box" with paper, crayons, colouring books or paper. Colour and draw lines and shapes with your child.

- Play matching games. Ask your child to find objects in books or around the house that are the same.

- Hold your child's hand going up and down stairs. When she can go up and down easily, encourage him/ her to use the railing.

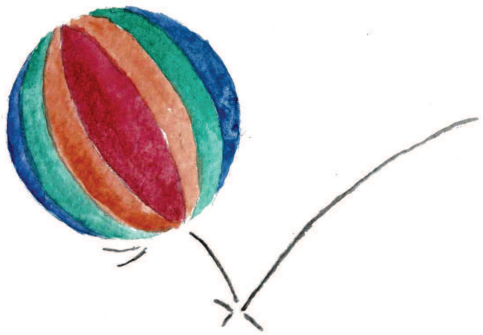
- Play outside with your child. Allow your child to play

Toys and items you can use at home:

- Small blocks (if you do not have blocks use a small empty match box).
- Cheerios' to practice small grasp.
- Cars and dolls.
- Balls.
- Everyday items e.g. comb, face cloth, cup, spoon etc.
- Hard cover picture books (if you do not have a picture book use a magazine with bright pictures and make a picture book).
- Paper and crayons or pencils. You can even use colouring in books if available.
- Connecting blocks (plastic block that stick and fit onto each other like Lego).
- Shape board with circle, square and triangle. If you do not have a shape board you can make your own out of a thick piece of cardboard from a shop box. Cut out a square board and copy the shapes included at the back of the document onto the cardboard.

Cut out matching shapes from another piece of cardboard. To make picking the pieces up easier stick on a plastic coke bottle lid.

- Matching pictures (cut out and stick on cardboard) or snap cards with pictures.
- Two piece puzzles (cut out a circle and colour in as a ball, stick it on cardboard and cut into two pieces).



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ACTIVITY GUIDELINE FOR INFANTS AND TODDLERS



36 – 42 MONTHS

WHAT BABIES SHOULD DO AT THIS AGE:

Physical development:

- Can keep their balance while kicking a ball.



- Can jump off a step and jump forward when standing on the ground.
- Can start walking up and down a few steps without a hand rail.
- Can balance for a few seconds when standing on one leg.
- Child can draw a Vertical (|) and a horizontal (__) line on a paper.
- Can string three blocks/ or rings on a string.
- Can snip a piece of paper with a child's scissors and cut along a line.
- Can button a big button with a large buttonhole.

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- Can start tracing shapes.
- Can stack six to eight blocks on top of each other or in a straight row.

Learning thinking and problem solving:

- Can match objects of the same colour e.g. red, yellow, and blue.
- Can match pictures.
- Can assemble a three or four piece puzzle.
- Can identify items in pictures correctly.
- Can use item in an imaginary way e.g. a ball as an apple, a block as soap.
- Can count in order from one to ten.
- Can match shapes.
- Can put a shoelace through small hole.

Language skills:

- Can follow two or three step instructions e.g. fetch the ball, bring it here, and put it in the basket.
- Can name most familiar objects.

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- Can name basic colours e.g. red, yellow, green, and blue.
- Understands concepts like “inside”, “on top” and “under”.
- Uses words like “I”, “me”, “we” and “you”.
- Uses plurals (multiples of objects) e.g. cars, cats, dogs, dolls.
- Can identify action e.g. waving, riding, eating, and sleeping.
- Uses two to three sentences to have a conversation, and strangers for the most part understand them.

Social and emotional skills:

- Copies adults and friends.
- Enjoys playing with friends more than playing alone.
- Enjoys games that involve make-believe or imaginary play.
- Dress and undress themself.
- Separates easily from parents.
- Enjoys new things.



You should be worried if your baby <u>does not</u>:

Cannot jump on one place.

- Does not pretend play.
- Has difficulty scribbling on a piece of paper or cutting.
- Is not interested in playing games.
- Does not gain new words, and communicates poorly
- Has difficulty playing with other children and does not make friends

- Does not follow instructions with more than one step
- Does not want to get dressed, use the toilet or want to sleep,
- Has trouble learning to dress and do buttons.
- Problems learning numbers.
- Over active
- Short attention span
- Loses skills that he/she had.

If you noticed any of the above problems immediately tell a nurse at your local clinic, a doctor, physiotherapist or occupational therapist

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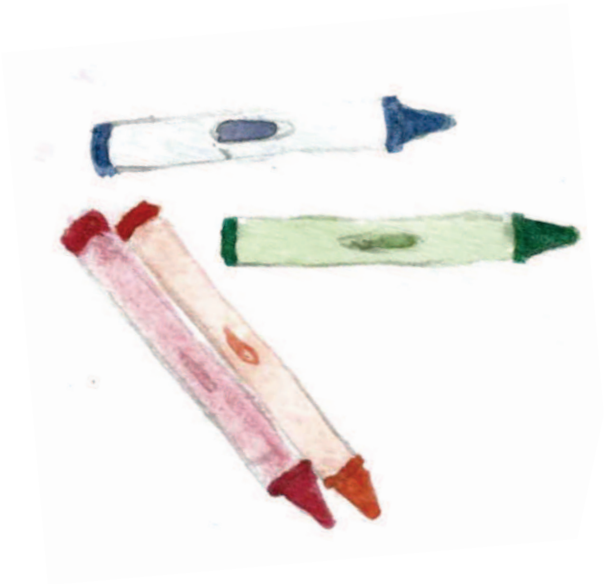


Things you can do to help your baby's development:

- Give your child instructions with two or three steps. For example, "Go to your room and get your shoes and coat."
- Read to your child every day. Ask your child to point to things in the pictures and repeat words after you.
- Give your child an "activity box" with paper, crayons, and colouring books. Colour and draw lines and shapes with your child. Practice tracing shapes and cutting along a line.
- Play matching games. Ask your child to find objects in books or around the house that are the same.
- Play make-believe with your child. Let her be the leader and copy what she is doing.
- Give your child simple choices whenever you can. Let your child choose what to wear, play, or eat for a snack. Limit choices to two or three options.
- During play dates, let your child solve her own problems with friends, but be nearby to help out if needed.
- Encourage your child to use words, share toys, and take turns playing games.
- Give your child toys that encourage them to use their imagination, like dress-up clothes, kitchen sets, and blocks.
- Use good grammar and language when speaking to your child. Instead of "Mommy wants you to come here," say, "I want you to come here."
- Use words like "first," "second," and "finally" when talking about everyday activities. This will help your child learn about sequence of events.
- Take time to answer your child's "why" questions. If you don't know the answer, say "I don't know," or help your child find the answer in a book, on the Internet, or from another adult.

- When you read with your child, ask him to tell you what happened in the story as you go.

- Ask your child to identify colours in books, pictures, and things at home.

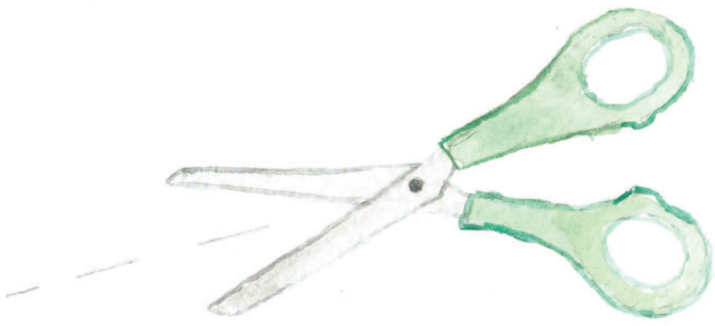
- Count common items, like the number of blocks, stairs, or toys.

- Teach your child to play outdoor games.

- Play your child's favourite music and dance with your child. Take turns copying each other's moves.

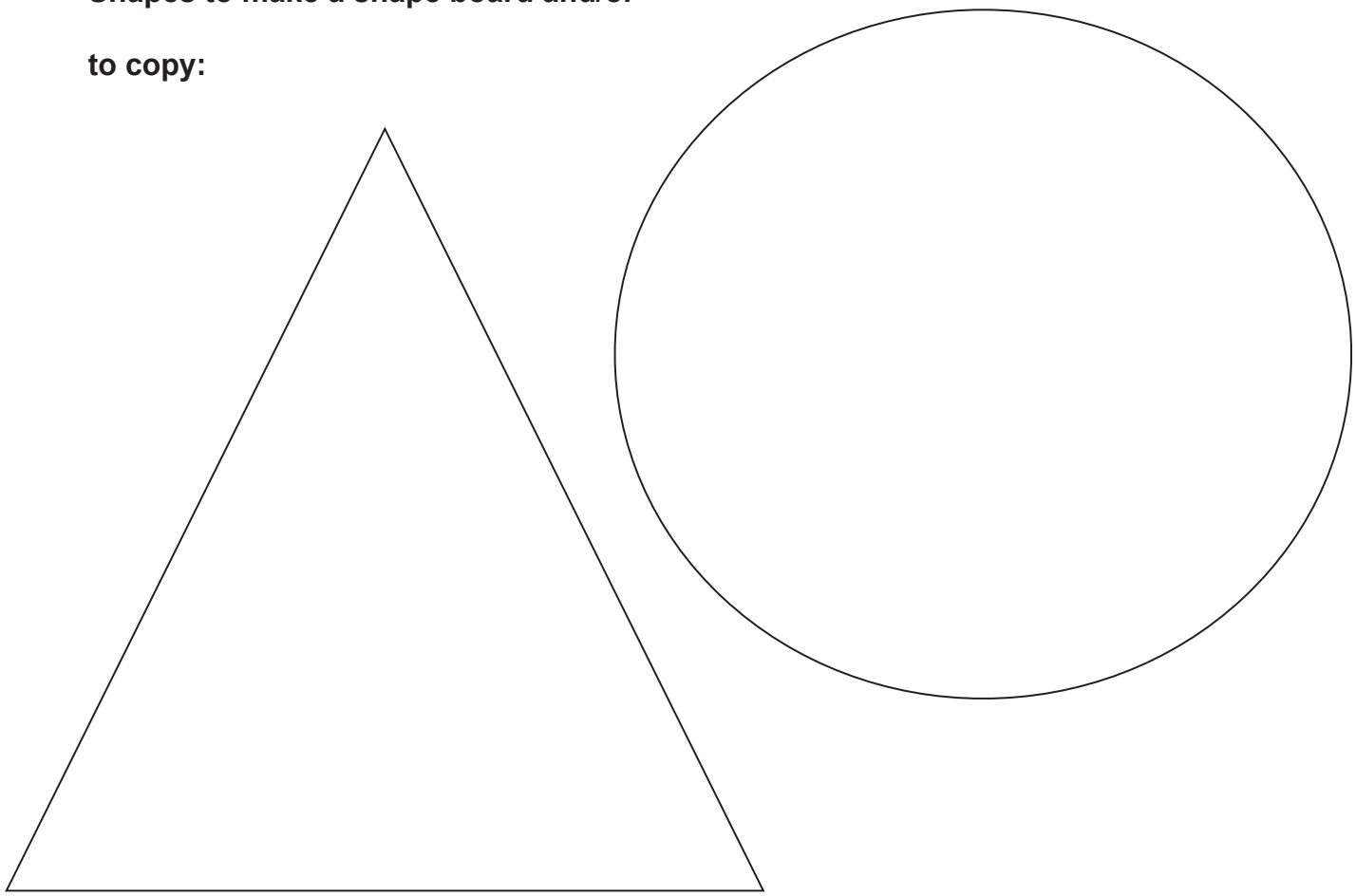
Toys and items you can use at home

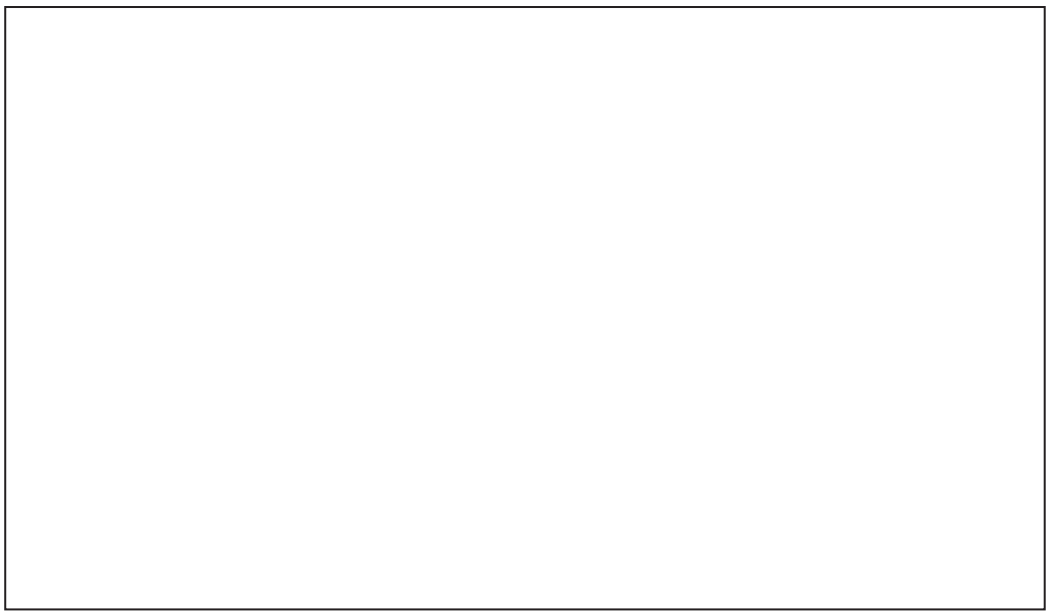
- Small blocks (if you do not have blocks use a small empty match boxes).
- Plastic connecter blocks.
- Cars and dolls.
- Balls.
- Everyday items e.g. comb, face cloth, cup, spoon etc.
- Hard cover picture books (if you do not have a picture book use a magazine with bright pictures and make a picture book)
- Paper and crayons or pencils. Shape outlines to trace (see at the back).
- Large pasta rounds, beads or toilet paper roll cut into pieces and a shoelace to string.
- Child safe scissors to practice cutting along a line (see at the back).
- Pictures to match or snap cards.
- Coloured items to match in red, yellow, blue and green.
- Three or four piece puzzles.



Shapes to make a shape board and/or

to copy:





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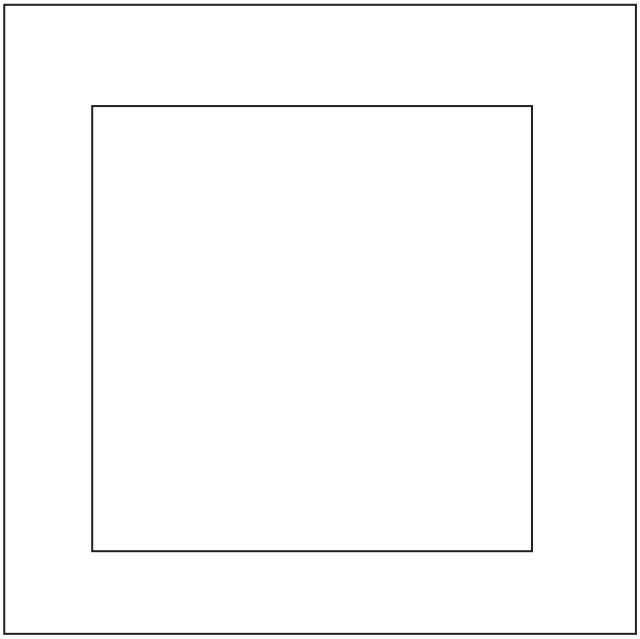
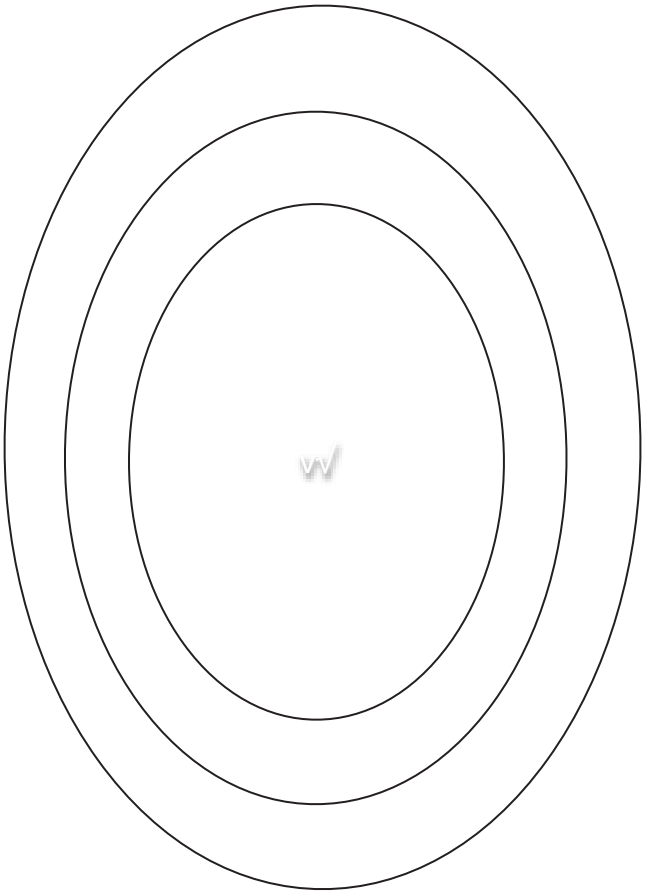
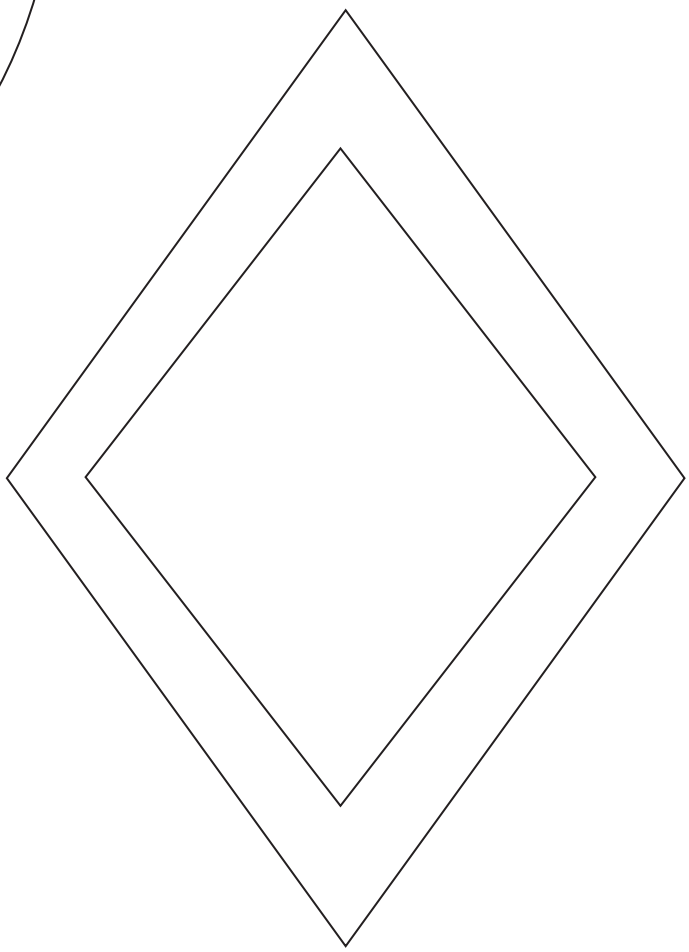
Shapes to draw between the lines:







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Lines to cut along with a pair of scissors:

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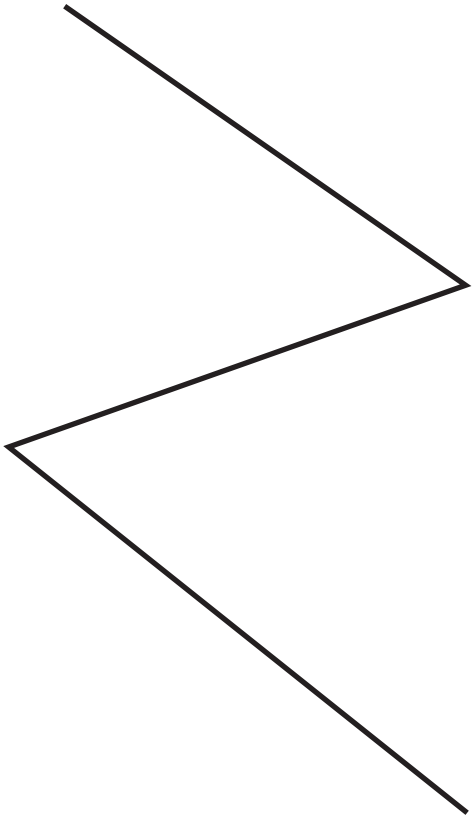
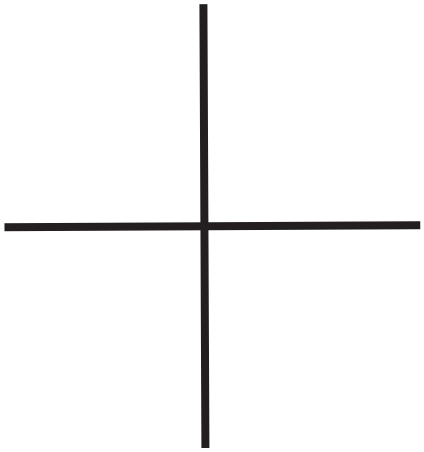
Lines to copy:





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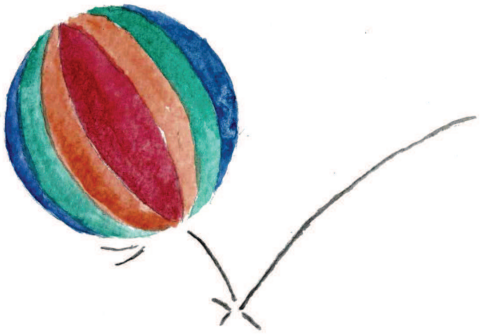
Reference documents

Pearson. 2006. Administration manual and record form of the Bayley Scales of Infant and Toddler Development. Third Edition.

Centre for Disease control and Prevention (CDC). Milestone moments. Learn the signs. Act early [available online].



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APPENDIX XXII

PROPOSED MODEL FOR IMPLEMENTATION OF THE DEVELOPMENTAL ACTIVITY PROGRAMME

APPENDIX XXII

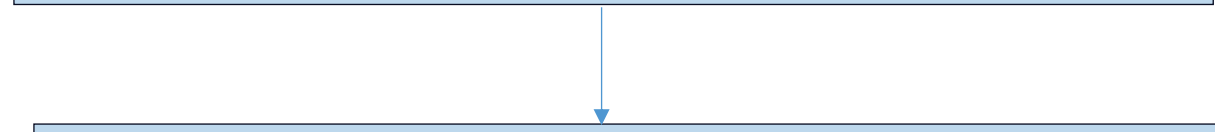
PROPOSED MODEL FOR IMPLEMENTATION OF THE DEVELOPMENTAL ACTIVITY PROGRAMME

STEP 1: CHILD ADMITTED FOR CARDIAC INTERVENTION

- Establish a collaborative relationship with family
- Initial developmental assessment of child (if possible), anddetermination of parental stress and perceived HRQOL of the child.
- Issue information document and explain post-operative precautions



STEP 2: CHILD UNDERGOES CARDIAC INTERVENTION



STEP 3: EDUCATION AND TRAINING SESSION BEFORE DISCHARGE

- Parents to attend a two-hour education and information session where the home-based developmental activity programme is initiated in line with the child's developmental assessment findings. Parents to be issued a logbook to monitor and encourage participation. Demonstration of developmental activities where indicated.
- Allow time for questions and encourage adherence. Clearly explain the principles to be applied with activity prescription, including the frequency, intensity and time (duration).
- Reaffirm precautions and activity limitations, provide clear time-frames for their application.
- Refer parents to support group (arrange for additional psychological support if required)



STEP 4: FOLLOW- UP AND EVALUATION EFFECTIVENESS OF THE PROGRAMME

- Send weekly text message reminders to parents to adhere to the home-based activity programme.
- Phone parents at least every second week at the initiation of programme implementation to answer any questions and update activities. Encourage parents to phone the therapist if they have any questions regarding the programme. Later,monthly follow-up is advised.
- The frequency of formal follow-up visits with the therapist will be determined by the developmental status of the child.
- Developmental re-evaluation is to be scheduled to coincide with cardiology follow-up or other hospital appointments (where possible at three-monthly intervals).
- Suggested follow-up timeframes for formal assessment of at-risk children: during the first year, again between three and five years, at school entry, again at middle school and during adolescence.

APPENDIX XXIII
TURNITIN SIMILARITY REPORT

APPENDIX XXIII

TURNITIN ORIGINALITY REPORT

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CHAPTER 1

INTRODUCTION

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