

https://dspace.org/

Fetal Alcohol Spectrum Disorder (FASD)

Davies, Leigh-Anne

2013-11-05
http://hdl.handle.net/10539/13301

Downloaded from a DSpace repository. https://dspace.org/

Fetal Alcohol Spectrum Disorder (FASD)

A LONGITUDINAL STUDY OF CHILDREN FROM INFANCY TO 5 YEARS OF AGE USING THE GRIFFITHS MENTAL DEVELOPMENTAL SCALES

LEIGH-ANNE DAVIES

A thesis submitted to the Faculty of Humanities, School of Human and Community Development, University of the Witwatersrand, Johannesburg, in fulfillment of the requirements for the degree of Doctor of Philosophy.

Johannesburg, 2013

Declaration

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

L Davies

_____day of _____, 2013

Dedication

To our little miracle, Colby Joe Davies.

"Many things can wait, the child cannot. Now is the time his bones are being formed, his blood is being made, his mind is being developed. To him we cannot say tomorrow, his name is today."

Gabriela Mistral, Chilean Poet

Acknowledgements

I am *indebted* to the following people who have travelled this path with me:-

To the families from the De Aar community, who touched my heart and changed my life.

Many thanks to all at The Foundation for Alcohol Related Research (FARR) in particular, Prof Denis Viljoen, Leana Olivier, Dr Candice Chetty, Zelia Gomes and the late Stefanie Schön for your support, professional advice and friendship over the years.

To the ladies at the Joan Wertheim Centre; Mabel, Sylvia, Lena, Annelise, Wendy, Lydia, Carol, Ntsiki and the late Nosipho, thank you for your commitment to the study.

To Prof Matthew Chersich and Dr Michael Urban for statistical advice, technical editing and academic support.

To my supervisor, Prof Kate Cockcroft for your invaluable contributions, expert advice and continued encouragement, I have learnt so much from you.

To my parents and family; thank you for your love and support. For all you do, all you are and all you make me!

Finally, to Lloyd for supporting me through the daunting abyss that is a PhD. Always loving, understanding and motivating, I could not have done this without you!

Abstract

Alcohol use during pregnancy is common and its consequences often result in a broad range of negative, lifelong developmental outcomes. This study describes the effects of prenatal alcohol exposure and interacting socio-demographic factors on early childhood development. One hundred and twenty one children from the Northern Cape, South Africa, were clinically examined using standard diagnostic procedures and assessed using the Griffiths Mental Development Scales (GMDS/ER) at 7-12 months (Time 1) and 5 years of age (Time 2). Participants were assigned to either: a Fetal Alcohol Syndrome (FAS/Partial Fetal Alcohol Syndrome (PFAS); a Prenatal Alcohol Exposed (PAE); or a Control group based on the diagnosis at 5 years. Mothers/caregivers were interviewed to ascertain socio-demographic information, including prenatal alcohol exposure. During infancy, the FAS/PFAS group showed significantly lower gross motor and language abilities, with delays in higher-order executive functioning becoming more apparent with age. No significant differences were noted during infancy between the PAE and Control groups over any developmental subscales. However, with age, higher-order executive function delays were reported in the PAE group. Performance on the infant and child versions of the GMDS was not significantly correlated, suggesting that the tests may be measuring different developmental constructs. Lower maternal education, unemployment and later recognition of pregnancy were associated with reduced social adaptive functioning, and language and eye hand coordination abilities, irrespective of amount of prenatal alcohol exposure over both time points. Larger anthropometric birth measurements and longer duration of

breastfeeding were significantly related to increased performance on the GMDS at 5 years within the groups exposed to prenatal alcohol. Socio–demographic variables are likely to complicate developmental profiles for all three groups, with prenatal and postnatal nutrition emerging as possible protective factors for positive developmental outcomes at 5 years of age.

Keywords: Fetal Alcohol Syndrome (FAS), Developmental Delay, Longitudinal, Socio-demographic factors

Table of Contents

Fetal Alcohol Spectrum Disorder (FASD) I

Declaration II

Dedication III

Acknowledgements IV

Abstract 1

Table of Contents 3

Table of Figures 8

List of Tables 11

Chapter 1 - Introduction 13

1.1 Introduction 13

Chapter 2 – Literature Review 21

2.1 Introduction 21

2.2 Historical Aspects 22

2.3 Diagnosing Fetal Alcohol Spectrum Disorder (FASD) 23

2.4 Structural and Functional Abnormalities Associated with Prenatal Alcohol Exposure (PAE) 30

2.4.1 Structural abnormalities. 30

2.4.2 Functional abnormalities. 33

2.5 Epidemiology of FASD 34

2.6 Risk factors associated with prenatal alcohol exposure (PAE). 35

2.7 Childhood Development 38

2.7.1 Motor skills. 39

2.7.2 Cognitive skills. 43

2.7.3 Language skills. 47

2.7.4 Social/emotional skills. 51

2.8 Cumulative Risk Factors Associated With Early Childhood Delays 55

Chapter 3 - Method 64

3.1 Introduction 64

3.2 Research Aims and Questions 65

3.2.1 Research question 1. 65

3.2.2 Research question 2. 66

3.2.3 Research question 3. 67

3.3 Research Design 67

3.4 Background to Sample 68

3.5 Sampling procedure 69

3.6 Assessments 72

3.6.1 Clinical diagnostic evaluation. 72

3.6.2 The infant and extended versions of the Griffiths Mental Developmental Scales (GMDS/ER). 74

3.6.3 The maternal interview. 80

3.7 Procedure 81

3.8 Statistical Analyses 85

Chapter 4 – Results 88

4.1 Descriptive Statistics 88

4.2 Inferential Statistics 95

4.2.1 Research question 1. 95

4.2.2 Research question 2. 104

4.2.3 Research question 3. 106

4.3 Conclusion 116

Chapter 5 – Discussion and Conclusions 118

5.1 Introduction 118

5.2 Developmental differences between groups with varying degrees of prenatal alcohol exposure 119

5.3 Relationship between infant performance and later achievement over developmental subscales of the GMDS/ER 130

5.4 Impact of socio-demographic variables on early childhood development 136

5.4.1 Infant characteristics. 136

5.4.2 Maternal characteristics. 141

5.4.3 Pregnancy and lifestyle characteristics. 144

5.5 Major findings and implications 150

5.6 Limitations 153

5.7 Conclusions 158

Reference List 159

List of Appendices 215

APPENDIX A: Ethics Clearance and Department of Health Approval 215

APPENDIX B: Clinical Examination and Consent Forms 218

APPENDIX C: Maternal Interview and Consent Form 226

APPENDIX D: Histogram Distributions for GMDS Infant Version Subscales at 7-12months (TIME 1) for FAS/PFAS Group 246

APPENDIX E: Histogram Distributions for GMDS Infant Version Subscales at 7-12months (TIME 1) for PAE Group 249

APPENDIX F: Histogram Distributions for GMDS Infant Version Subscales at 7-12months (TIME 1) for Control Group 252

APPENDIX G: Histogram Distributions for GMDS/ER Version Subscales at 5 years (TIME 2) for FAS/PFAS Group 255

APPENDIX H: Histogram Distributions for GMDS/ER Version Subscales at 5 years (TIME 2) for PAE Group 259

APPENDIX I: Histogram Distributions for GMDS/ER Version Subscales at 5 years (TIME 2) for Control Group 263

Table of Figures

Figure 1. Bronfenbrenner's Ecological Model of Child Development 57

Figure 2. Pathways connecting cumulative risk factors and poor child development 59

Figure 3. Recruitment and attrition of participants for the study 71

Figure 4. Developmental achievement between the FAS/PFAS (n = 24) and Control (n = 36) groups over Time 1 and Time 2 101

Figure 5. Developmental achievement of the PAE (n=56) and Control groups (n=36) over Time 1 and Time 2 102

Figure 6. Histogram of Locomotor subscale at Time 1 246

Figure 7. Histogram of Personal-Social subscale at Time 1 246

Figure 8. Histogram of Language subscale at Time 1 247

Figure 9. Histogram of Eye-Hand Coordination subscale at Time 1 247

Figure 10. Histogram of Performance subscale at Time 1 248

Figure 11. Histogram of General Quotient at Time 1 248

Figure 12. Histogram of Locomotor subscale at Time 1 249

Figure 13. Histogram of Personal-Social subscale at Time 1 249

Figure 14. Histogram of Language subscale at Time 1 250

Figure 15. Histogram of Eye-Hand Coordination subscale at Time 1 250

Figure 16. Histogram of Performance subscale at Time 1 251

Figure 17. Histogram of General Quotient at Time 1 251

Figure 18. Histogram of Locomotor subscale at Time 1 252

Figure 19. Histogram of Personal-Social subscale at Time 1 252

Figure 20. Histogram of Language subscale at Time 1 253

Figure 21. Histogram of Eye-Hand Coordination subscale at Time 1 253

Figure 22. Histogram of Performance subscale at Time 1 254

Figure 23. Histogram of General Quotient at Time 1 254

Figure 24. Histogram of Locomotor subscale at Time 2 255

Figure 25. Histogram of Personal-Social subscale at Time 2 255

Figure 26. Histogram of Language subscale at Time 2 256

Figure 27. Histogram of Eye-Hand Coordination subscale at Time 2 256

Figure 28. Histogram of Performance subscale at Time 2 257

Figure 29. Histogram of Practical Reasoning subscale at Time 2 257

Figure 30. Histogram of General Quotient at Time 2 258

Figure 31. Histogram of Locomotor subscale at Time 2 259

Figure 32. Histogram of Personal-Social subscale at Time 2 259

Figure 33. Histogram of Language subscale at Time 2 260

Figure 34. Histogram of Eye-Hand Coordination subscale at Time 2 260

Figure 35. Histogram of Performance subscale at Time 2 261

Figure 36. Histogram of Practical Reasoning subscale at Time 2 261

Figure 37. Histogram of General Quotient at Time 2 262

Figure 38. Histogram of Locomotor subscale at Time 2 263

Figure 39. Histogram of Personal-Social subscale at Time 2 263

Figure 40. Histogram of Language subscale at Time 2 264

Figure 41. Histogram of Eye-Hand Coordination subscale at Time 2 264

Figure 42. Histogram of Performance subscale at Time 2 265

Figure 43. Histogram of Practical Reasoning subscale at Time 2 265

Figure 44. Histogram of General Quotient at Time 2 266

List of Tables

Table 1 Summary of diagnostic classification of FASD 26

Table 2 Piaget's Four Stages of Cognitive Development 40

Table 3 Early Language Milestones 49

Table 4 Erikson's Epigenetic Sequence of Psychosocial Development 53

Table 5 Infant Characteristics based on Group Allocation (N=121) 89

Table 6 Maternal Characteristics based on Group Allocation (N=121) 90

Table 7 Pregnancy and Lifestyle Variables based on Group Allocation (N=121) 91

Table 8 Descriptive Statistics for groups over the GMDS subscales at Time 1 93

Table 9 Descriptive Statistics for groups over the GMDS/ER subscales at Time 2 94

Table 10 Kruskal–Wallis Summary Table of Differences between Groups at 7-12 months of age, Time 1 96

Table 11 Kruskal–Wallis Summary Table of Differences between Groups at 5 years of age, Time 2 98

Table 12 Group Differences between Time 1 and Time 2 Assessments 100

Table 13 Intercorrelations between subscales of the GMDS and GMDS-ER over time 105

Table 14 Correlations between infant variables and developmental performance over GMDS subscales at Time 1 107

Table 15 Correlations between maternal variables and developmental performance over GMDS subscales at Time 1 108

Table 16 Correlations between maternal lifestyle and pregnancy variables and developmental performance over GMDS subscales at Time 1 110

Table 17 Correlations between baseline infant variables and developmental performance over GMDS/ER subscales at Time 2 111

Table 18 Correlations between maternal variables and developmental performance over GMDS/ER subscales at Time 2 113

Table 19 Correlations between maternal lifestyle and pregnancy variables and developmental performance over GMDS/ER subscales at Time 2 115

Chapter 1 - Introduction

Everything has been thought of before, but the difficulty is to think of it again.

Goethe

1.1 Introduction

Alcohol use during pregnancy is common in many parts of the world, and its consequences on early childhood development are of great international importance (Lewis et al., 2012). While most women abstain from alcohol following confirmation of their pregnancy; some continue to drink low-to-moderate, even heavy amounts throughout (Henderson, Gray & Brocklehurst, 2007). With about half of all pregnant women recognising their pregnancy after the sixth week, an estimated 15-50% of fetuses are likely exposed to some level of alcohol in utero (Ebrahim et al, 1998, Floyd, Decoufle & Hungerford, 1999; Floyd, Ebrahim, Boyle & Goule, 1999). Higher rates of exposure are probable in communities with increased alcohol use.

Findings of whether a safe level of prenatal alcohol exposure (PAE) exists are controversial. Some recent studies suggest that low-to-moderate amounts of alcohol during pregnancy do not affect children's behaviour or IQ during childhood (Robinson et al., 2010; Falgreen Eriksen et al., 2012). Other research, however, proposes that even small quantities of prenatal alcohol exposure negatively impacts child behaviour (Larkby & Day, 1997; Sood et al., 2001; Stoler & Holmes, 2004).

Structural, cognitive and behavioural effects of alcohol are contingent on the intensity, timing and pattern of maternal alcohol consumption during critical periods of fetal development (Abel, Kruger & Friedl, 1998; Hoyme et al., 2005; May, Gossage, Brooke et al., 2005; May, Gossage, Marais et al.,2007; Stratton, Howe & Battaglia, 1996; Sulik, 2005; Sulik, Johnston & Webb, 1981; Urban et al., 2008; Viljoen, Croxford et al., 2002; Viljoen, Gossage et al., 2005). Heavy alcohol consumption in pregnancy is linked to a set of distinct dysmorphological and behavioural difficulties in exposed fetuses, referred to as Fetal Alcohol Syndrome (FAS). While light-to-moderate levels of prenatal alcohol exposure may not produce the typical Fetal Alcohol Syndrome (FAS) phenotype, drinking at such levels could result in subtle to significant central nervous system (CNS) impairments, manifesting in a variety of developmental delays, forming sub diagnoses under the broader Fetal Alcohol Spectum Disorder (FASD) (Riley & McGee, 2005; Sampson, Streissguth, Bookstein & Barr, 2000).

International prevalence rates of FASD vary and are likely a reflection of variations in study populations, case definition, case ascertainment sources, and surveillance methodologies among studies, making it difficult to establish an accurate international incidence of FASD. According to a summary of various studies conducted in the United States, May and Gossage (2001) report overall prevalence rates of FAS between 0.5 and 2.0 per 1,000 with subsequent estimates that FASD affects 1 in 100 people (Carmichael-Olson et al., 2009; May & Gossage, 2001). Recent Italian findings suggest FASD prevalence rates of 2.3% to 6.3% amongst children, substantially higher than previous estimates of overall FASD for the general populations of Western Europe and the U. S (May et al., 2011). South Africa have amongst the highest reported FAS rates worldwide, with levels between 40.5 to 119.4 per 1000 in various South African communities

(Chersich et al., 2012; May, Gossage, Brooke et al., 2005, May, Gossage, Marais et al., 2007; Viljoen et al., 2005; Urban et al., 2008).

The true epidemiology of FASD is unknown with many cases of FASD remaining undetected (Hoyme et al., 2005). Frequent misdiagnoses during childhood, further complicate prevalence rates and are likely due to the absence of the typical FAS facial features attributed to maternal abstinence from alcohol during the first trimester when facial features develop (Mattson, Riley, Gramling, Delis & Jones, 1997). Children with prenatal alcohol exposure (PAE) often present with a complex diagnostic picture and a wide range of psychological symptoms with reported diagnoses which include; attention deficit hyperactivity disorder (ADHD), depression, oppositional defiant disorder, conduct disorder, anxiety disorders, obsessive compulsive disorder and bipolar disorder (Burd, Klug, Martsolf & Kerbeshian, 2003; Mattson & Riley, 2000). While an early identification during infancy is controversial, with studies differing in opinion of whether it is possible, the early diagnosis of FASD has proven an important protective factor for individuals with FASD, with children diagnosed prior to the age of 6 years reporting less secondary disabilities (Davies et al., 2011; Hoyme et al., 2005; Burd et al., 2003; Streissguth, Barr, Kogan, Bookstein, 1996). Due to these and other difficulties, recent research is shifting from mainly clinical studies to those identifying behavioural and neurobehavioural signs, as well as genetic markers, usually more pronounced amongst children with FASD (Aragon et al., 2008; Carr, Agnihotri & Keightley, 2010; Hong & Krauss, 2012; Quattlebaum & O'Connor, 2012).

While findings confirm that FASD is often the result of a complex interaction between diverse social, political, environmental and genetic risk factors they further fortify that children,

regardless of prenatal alcohol exposure, develop in relation to their environment and not in isolation to it (Bronfenbremmer, 1979; Bronfenbrenner & Ceci, 1994). Socio–demographic factors further complicate the accurate identification and management of early developmental deficits, especially over sensory–motor, cognitive–language and social functioning with socio-economic deprivation or living in low-or middle-income countries itself linked to developmental delays (Cockcroft, Amod & Soellart, 2008; Gale, O'Callaghan, Bredow, Martyn & Avon Longitudinal Study of Parents and Children Study Team , 2006; Grantham-McGregor et al., 2007; Hack, Klein & Taylor, 1995; Richards, Hardy, Kuh & Wadsworth, 2002; Shenkin, Starr & Deary, 2004). In South Africa, large sections of the population suffer from poverty and are disadvantaged, in poorly resourced communities, therefore at particular risk to poor cognitive development failing to achieve their developmental potential. Children living in poverty are exposed to increasing numbers of risks over time with the cumulative effects of these risk factors becoming more evident as children get older (Grantham-McGregor et al., 2007; Laughton et al., 2010). Factors such as, pre and postnatal nutrition, low birth weight, socio-economic status (SES), level of maternal education, parental employment, maternal age, body mass index (BMI) maternal age, parity, maternal depression and parenting styles have all been well researched within the context of early childhood development (Baker–Henningham, Powell, Walker & Grantham–McGregor, 2003; Beaver, Vaughn, DeLisi & Higgins, 2010; Coles, Platzman, Smith, James & Falek, 1992; Daniels & Adair, 2005; Gale et al., 2006; Grantham–McGregor, et al., 2007; Richards et al., 2002; Jain, Concato & Leventhal, 2002, Khaole, Ramchandani & Viljoen, 2004; Urban et al., 2008).

While developmental delay in children with FAS in high-income countries has been well documented, there is considerably less evidence from non-Western, resource-constrained countries with few drawing comparisons with an appropriate control group (e.g. Adnams et al., 2001; Mattson et al., 1997). It is thus critical, when studying the development of alcohol-exposed children from low socio-economic circumstances (the environments in which affected children typically are found), that their development be compared to that of healthy children from the same environment (Coles, 1995; Grantham-McGregor et al., 2007). This becomes even more important in non-Western communities where developmental measures commonly used to gauge typical development have not been normed or standardised. Not only will this research contribute to existing knowledge of developmental deficits amongst children living in impoverished communities, exposed to alcohol prenatally, but it aims to provide valuable information regarding the correlational use of both Infant and Child versions of GMDS/ER in a unique sample of children.

An accurate assessment of a child's development requires a thorough assessment, which should measure a child's physical, cognitive, social and emotional development (Bondurant-Utz & Luciano, 1994; Meisels, 1996; Nuttal, Romero & Kalesnik, 1992). Developed by Ruth Griffiths in the United Kingdom in 1954, The Griffiths Mental Development Scales (GMDS) was designed to assess the overall development of babies from birth to 2 years and children from 2-8 years over six domains of functioning, namely; Locomotor, Personal-Social, Language, Eye and Hand Coordination, Performance and Practical Reasoning (included in the 2-8year version) (Griffiths, 1954; 1970; 1986). Recent versions of the GMDS have been revised and extended to offer a more comprehensive developmental measure (Huntley, 1996; Luiz, Foxcroft & Povey,

2006). In both versions, each subscale was devised to be a separate and complete scale in itself, measuring one process of development completely (Griffiths, 1970; 1986). International research using the GMDS/ER has been conducted in a number of countries including South Africa, with findings confirming their practical and diverse uses in the evaluation and treatment of infants and young children from a variety of cultural backgrounds (Allan, 1988; 1992; Barnard, 2000; 2003; Bhamjee, 1991; Cockroft et al., 2008; Knoesen, 2003, 2005; Kotras, 1998; 2003; Luiz, 1988a; 1988b; 1988c; 1988d; Luiz, Foxcroft & Povey, 2006; Luiz, Foxcroft & Stewart, 2001; Luiz, Foxcroft, Worsfold, Kotras & Kotras, 2001; Luiz & Heimes, 1994; Moosajee, 2007; Tukulu, 1996; Van Rooyen, 2005; Ward, 1997).

Over the years, the usefulness of the GMDS/ER in the assessment of children with various disorders and disabilities has been indicated by clinical studies. Studies include those of children with Attention Deficit Hyperactivity Disorder (ADHD), Autism, Cerebral-Palsy, Down's Syndrome, Fetal Alcohol Syndrome (FAS), Muscular Dystrophy, Spina-Bifida, Hearing impaired and HIV^+ infants (Adnams et al., 2001; Beail, 1985; Bidder, Bryant & Gray, 1975; Cohen, 2003; Hall, 1971a; 1971b; Houston-McMillan, 1988; Krige, 1988; Ludlow, 1980; Ludlow & Allen, 1979; Luiz, 1988b; Piper & Pless, 1980; Sandberg, Nyden, Gillberg, & Hjelmquist, 1993; Sandison, 2005; Smith, Sibert & Harper, 1990; Spain, 1970; Welbourn, 1975).

Studies conducted in South Africa have contributed to restructuring the items on the revised editions making them non-threatening and reasonably culturally fair with reported cultural developmental differences explained by external variables, such as socio-economic status (SES) and levels of maternal education (Cockcroft, et al., 2008; Houston-McMillan, 1988). With the

alpha coefficient reaching 0.993, the GMDS-ER provides particularly favourable reliability findings; with studies on content and construct–related evidence providing further validation of it as a valid diagnostic developmental test (Smith, Bidder, Gardner & Gray, 1980; Griffiths, 1986; Hanson, 1982; Huntley, 1996; Luiz et al., 2006). While studies indicate low test-retest reliability, under a year of age on the Infant Scale, findings emerge as highly reliable from the second year onwards (Huntley, 1996). Though the validity and reliability of both the Infant and Child versions of the GMDS/ER have been proven and are fairly well researched, less is known of the association between constructs of the Infant and Extended Versions of the GMDS/ER. Findings conducted by Luiz and colleagues (2001) describe how all subscales tap the same underlying construct, namely, general intelligence, which appeared to be consistent across cultures. Furthermore, their findings indicated overlaps in constructs being assessed over time, with certain constructs common amongst all subscales (Luiz et al., 2001; Povey, 2008). The current study provides a unique longitudinal opportunity to report on the associations between subscales across versions of the GMDS/ER over time. While developmental studies are usually longitudinal in nature, many existing prenatal studies have been cross-sectional and/or correlational in nature. Longitudinal studies such as this one are therefore needed to assist in the early identification of developmental delay associated with prenatal alcohol exposure and socio-demographic factors.

Therefore, the main purpose of this thesis was to describe and explore the development of three groups of children from an impoverished town in South Africa, those diagnosed with FAS/PFAS; those with some prenatal exposure but who don't meet the criteria for a FASD diagnosis; and a control group of children from the same community (with no FASD

symptomatology or no to low reported prenatal alcohol exposure prior to pregnancy). By comparing these three groups, the study examines both the separate and cumulative effects of varying degrees of prenatal alcohol exposure and socio-demographic factors, on developmental outcomes during the first five years of childhood.

The following chapters set the context for understanding the current study and its findings. The second chapter covers the broader topic of early childhood development, with specific reference to the impact both; prenatal alcohol exposure (PAE) and socio-demographic factors, have on the first five years of childhood development. Chapter 3 provides the methods employed in conducting the study, including the aims, rationale of the research and a brief description of the statistical procedures utilised with the results of the current study presented in Chapter 4. Finally, Chapter 5 provides an integrated discussion of the findings, as well as providing limitations of the study and some indication of the direction for future research.

Chapter 2 – Literature Review

We never think entirely alone: we think in company, in a vast collaboration; we work with the workers of the past and of the present.

A.D. Sertillanges

2.1 Introduction

Increased media coverage regarding the dangers of alcohol use, abuse and binge drinking may suggest the threats associated with drinking alcohol during pregnancy are new. While the effects of alcohol during pregnancy have been cautioned throughout history, its interruption with embryonic and fetal development were only recognised fairly recently in the late 20th century (Jones & Smith, 1973; Jones, Smith, Ulleland & Streissguth, 1973; Lemoine et al., 1968; Sullivan, 1899). Remarkable advances in our understanding of these teratogenic effects of alcohol have since taken place and it is now widely accepted that children exposed to substantial amounts of alcohol during pregnancy exhibit a range of physical, cognitive and behavioural outcomes, collectively referred to as Fetal Alcohol Spectrum Disorders (FASD) (Hoyme et al., 2005; Mattson et al, 1997).

The present chapter reviews the diagnostic criteria required for a FASD diagnosis, describes structural and functional abnormalities associated with prenatal alcohol exposure and provides information regarding its influence over early childhood developmental abilities. Further

attention is placed on the cumulative influence of other socio-demographic factors, often present amongst communities with high rates of FASD, on early childhood development.

2.2 Historical Aspects

Used and valued by civilisations for thousands of years, alcohol formed part of cultural, medical and religious practices, which ironically was once fostered during pregnancy to improve maternal nutrition and accepted as a treatment for premature labour and a painkiller of the childbirth (Warner & Rosett, 1975). The passing of the "Act for the Encouraging of the Distillation of Brandy and Spirits from Corn" in 1690 saw England actively promote gin production to utilise surplus grain and raise revenue, developing a "natural, controlled experiment" with devastating health and social effects referred to as the "Gin Epidemic" (Abel, 2001). Cheap, distilled gin flooded the market becoming the drink of choice amongst poor and working class alike, with writers at the time describing children born to gin-drinking mothers as "fragile, weak and withered" (George, 1966). Similar descriptions of babies of mothers who drank heavily were described years later referring to them as "starved, shrivelled and imperfect as though...numbered by many years" (Harrison, 1967).

Findings from studies conducted in the mid-eighteenth century first describe a link between institutionalized patients and neonatal deaths to parental alcoholism (Sullivan, 1899). Limited studies were published between the 1950's and 1960's with Lemoine and colleagues (1968) first describing a cluster of clinical features amongst infants from alcohol dependent women, as being of low birth weight and intelligence, short height, slow growth with language and psychomotor delay. Similar findings relating to infant failure to thrive associated with maternal alcohol consumption were subsequently confirmed by American researchers, with the distinguishing

cluster of features associated with heavy prenatal alcohol exposure named as that of Fetal Alcohol Syndrome (Jones et al., 1973). Based on only 11 cases their findings described the features associated with extreme and atypical drinking patterns, sparking a global interest in the impact of maternal alcohol consumption during pregnancy (Jones et al., 1973).

2.3 Diagnosing Fetal Alcohol Spectrum Disorder (FASD)

Recognized as the foremost preventable, non-genetic cause of intellectual impairment, Fetal Alcohol Syndrome (FAS) is more prevalent than Down syndrome and Autism (Abel, 1995; Clarke & Gibbard, 2003). The terminology and diagnostic classification of prenatal alcohol exposure have evolved and changed since the first identification of Fetal Alcohol Syndrome (FAS) (Jones & Smith, 1973; Lemoine et al., 1968). Studies confirm patterns of malformations associated with substantial amounts of alcohol during pregnancy with evidence emerging of a spectrum of structural and behavioural outcomes (Beattie, Day, Cockburn & Garg, 1983; Halliday, Reid & McClure, 1982; Majewski, 1981; Olegard et al., 1979; Rosett, 1980). While differences exist between the four commonly used diagnostic schemas all include anomalies in three distinct areas namely; prenatal/postnatal deficiency; central nervous system (CNS) dysfunction; and the characteristic pattern of facial anomalies (Astley & Clarren, 2000 (4-digit code); Bertrand et al., 2005 (National Task Force/CDC); Chudley et al., 2005 (Canadian Guidelines); Hoyme et al., 2005; Stratton et al., 1996 (Revised IOM).

It soon became apparent that FAS represented merely the tip of the proverbial ‘iceberg’ with a majority of alcohol exposed children being misdiagnosed as a result of the absence of the classic facial characteristics. While heavy alcohol consumption during pregnancy is linked with a set of

dysmorphological and behavioural difficulties in exposed fetuses, referred to as Fetal Alcohol Syndrome (FAS) less is known of the impact of light to moderate levels of prenatal alcohol exposure (Kodituwakku, 2010). Absence of the typical FAS facial features (one of the main criteria) may be attributed to maternal abstinence from alcohol during the first trimester, when facial features develop (Mattson et al., 1997; Moore & Persuad, 1993). Over the past thirty years, a number of publications have documented the teratogenic effects of alcohol on the developing central nervous system concurring that the effects of alcohol are not isolated to a particular trimester (Samson, 1986; Streissguth & O'Mailey, 2000; Little, Graham, Samson, 1982). This results in children with confirmed prenatal alcohol exposure, manifesting a variety of developmental delays, but who do not display the classic FAS features (Streissguth & O'Malley, 2000; Sampson et al., 2000). Due to the absence of the typical clinical features associated with FAS and the complex nature of developmental delays related to prenatal alcohol exposure, children with subtler physical features may never be diagnosed or receive misdiagnoses (Little, Snell, Rosenfeld, Gilstrap & Gant, 1990). The earliest age at which a clinical FASD diagnosis can be made is controversial with some researchers believing it is impossible to make a clinical diagnosis before 2 years of age (Burd et al., 2003; Larkby & Day, 1997). Infants with FAS, therefore, often go undetected till childhood, with most being diagnosed between 2 and 7 years of age when behavioural and cognitive delays become more apparent.

A non-diagnostic umbrella term, Fetal Alcohol Spectrum Disorder (FASD) was created recognising the range of outcomes associated with prenatal alcohol exposure (PAE), including; terms such Partial FAS (PFAS), Alcohol Related Birth Defects (ARBD) and Alcohol Related Neurodevelopmental Disorder (ARND) (Bertrand et al. 2005; Hoyme et al., 2005; Stratton et al.,

1996). Fetal Alcohol Spectrum Disorder (FASD) broadly refers to the physical, mental and/or behavioural outcomes and disabilities which may occur amongst individuals exposed to varying degrees of prenatal alcohol (Hoyme et al., 2005). This term has come to include other conditions thought to be related to prenatal alcohol exposure such as, spontaneous abortion (Kline, Shrout, Stein, Susser & Warburton, 1980) and sudden infant death (Klug, Burd, Kerbeshian, Benz & Martsolf, 2003). Clinical features of the FASD spectrum, as used by the current study are described in Table 1(Hoyme et al., 2005; IOM, 1996).

According to the criteria, children displaying the facial phenotype (including small palpebral fissures, midface hypoplasia, smooth philtrum and thin vermilion border); growth deficiency (≤10th percentile for height, weight or head circumference) and evidence of central nervous system (CNS) abnormalities were diagnosed with FAS. Those displaying some, but not all facial features with growth retardation, neurological abnormality or abnormal neurocognitive assessment were clinically diagnosed as Partial FAS (PFAS). Even in the absence of a history of maternal alcohol consumption in pregnancy, clinical diagnoses of FAS and PFAS are considered distinctive (Hoyme et al., 2005). While not used in the current study, the terms Alcohol Related Birth Defects (ARBD) and Alcohol Related Neurodevelopmental Disorder (ARND), ensure the inclusion of physical or behavioural conditions linked to prenatal alcohol exposure which often co-occur.

The misunderstanding exists that FAS is on the extreme negative end of the spectrum with ARND representing less negative effects, yet effects of prenatal alcohol exposure can be as damaging for individuals in the ARND group, due to the irreversible damage to the central nervous system CNS (Mattson & Riley, 1998).

Table 1

Summary of diagnostic classification of FASD

	Fetal Alcohol Spectrum Disorder			
	Fetal Alcohol Syndrome (FAS)	**Partial Fetal Alcohol Syndrome (PFAS)**	**Alcohol Related Birth Defects (ARBD)**	**Alcohol Related Neurodevelopmental Disorder (ARND)**
Facial Characteristics	≥2 of the following: short palpebral fissures (<10th percentile), thin vermillion border, smooth philtrum	≥2 of the following: short palpebral fissures (≤10th percentile), thin vermillion border, smooth philtrum	2 of the following: short palpebral fissures (≤10th percentile), thin vermillion border, smooth philtrum	
Growth Deficiency	Height or weight ≤10th percentile	Either height or weight (≤10th percentile) OR		
CNS involvement	Head circumference (OFC) ≤10th percentile or structural brain abnormality	Head circumference ≤10th percentile or structural brain abnormality or behavioural and cognitive abnormalities inconsistent with developmental level		Either 1) structural brain anomaly or OFC ≤ percentile or 2) evidence of a complex pattern of behavioural or cognitive abnormalities inconsistent with developmental level that cannot be explained by genetics, family background or environment alone
Minor abnormalities			Display 2 minor abnormalities: Cardiac, skeletal, renal, eyes, ears, other	
Alcohol Exposure	Confirmed or Not confirmed	Confirmed or Not confirmed	Confirmed	Confirmed

Source: Hoyme, E.H., May, P.A., Kalberg, W. O., Kodituwakku, P., Gossage, J. P., Trujillo, P. M., Buckley, M. A., Miller, J. H., Aragon, A. S., Khaole, N, Viljoen, D. L., Jones, K. L., & Robinson, L. K. (2005). A Practical Clinical Approach to Diagnosis of Fetal Alcohol Spectrum Disorders: Clarification of the 1996 Institute of Medicine Criteria. Paediatrics, 115 (1), 39-47

In a longitudinal study conducted by Greenbaum, Nulman, Rovet and Koren (2002) they suggest ARND is a significant disorder in its own right. Regardless of the extent of prenatal alcohol exposure, common to all individuals on the spectrum are the adverse and variable outcomes of central nervous system damage, with varying cognitive, behavioural and psychosocial manifestations, which change with age and circumstances (Riley & McGee, 2005; Streissguth et al., 1991; Streissguth, Barr, Sampson & Bookstein, 1994). In contrast to the evolving FAS facial features and growth deficiencies, the abnormalities associated with the central nervous system (CNS) persist throughout an individual's lifespan manifesting at different developmental

milestones with children with FAS failing to catch up developmentally and often remaining small in height, weight and head circumference measurements (Streissguth, 1997).

Research has shown that the facial features and growth deficiencies of FAS often change with age and vary between ethnic populations (Abel & Hannigan, 1995; Streissguth et al., 1996; May et al., 2010). In their review, Abel and Hannigan (1995) found no evidence suggesting that biological factors were responsible for the increased risk of FAS in African and Native American alcoholic women. In South Africa, particularly high rates of FASD have been reported amongst the mixed ethnic, coloured communities (May et al., 2010; Viljoen et al., 2002; Urban et al., 2008). While research has shown increased prevalence of FAS amongst certain indigenous racial groups it may have less to do with racial characteristics and genetics and more to do with socio-economic status (SES) and drinking patterns (May et al 2010; O'Leary, 2004). It is important to note that aspects specific to indigenous populations, such as the effects of colonization, marginalisation and loss of traditional culture, may further impact the number of risk factors indicative of not only FASD but overall delays during early childhood development (Elliot & Bower, 2004).

As if the complex nature of diagnosing FASD was not enough, more women drink alcohol during pregnancy than the total number of children diagnosed within the FASD spectrum (Maier & West, 2001a). Thus, not all children prenatally exposed to alcohol will be diagnosed with FASD, with the degree of severity of prenatal damage varying from person to person. Effects of alcohol and their degree on subsequent developmental outcomes seem contingent on the

intensity, timing and pattern of maternal alcohol consumption during critical periods of fetal development (Autti-Ramo & Granstom, 1991, Guerri, Bazinet & Riley, 2009; Jacobson & Jacobson, 1999; Larroque, Kaminski, Deaene, Subtil, Delfosse & Querleu, 1995; Lindsley, Comstock & Rising, 2002; Mattson, Schoenfield & Riley, 2001; McCarver, 2001; Riley & McGee, 2005). In a prospective study conducted by Plant (1985) of 1,008 pregnant women in Scotland, women consuming ten units of alcohol or more on a single occasion during pregnancy were more likely than other women to produce damaged offspring. Evidence further indicated that low levels of maternal consumption were not associated with fetal harm. Plant claimed that the use of mild to moderate levels of alcohol during pregnancy appeared far less responsible for birth abnormalities than other factors such as; socio-economic status, maternal age, previous obstetric history, maternal height.

While the central nervous system (CNS) continues to develop during the 9 months of pregnancy, damage to particular regions of the developing brain at key points, due to heavy drinking, may result in global, functional and developmental delays. According to O'Leary (2004) a critical period for the damaging effects of heavy alcohol consumption occurs in the first 3-6weeks of brain development and the last 2 months of pregnancy. Maier and West (2001a, b) confirm this, stating that earlier exposure to alcohol in utero produces as much adverse effects on fetal brain development as alcohol exposure throughout pregnancy. About half of all pregnant women only recognize their pregnancy after the sixth week, a critical time for early brain development, with an estimated 15-50% of all fetuses exposed to alcohol in utero (Ebrahim et al., 1998, Floyd et al., 1999). While most women abstain from alcohol following confirmation of their pregnancy, some continue to drink low to moderate amounts throughout (Henderson et al., 2007). Conflicting

reports in the media regarding alcohol units and pregnancy guidelines during pregnancy further complicate opinions of alcohol use during pregnancy. In most developed countries, pregnancies are planned, complications few and outcomes generally favourable for both mother and infant. Research in developing countries is more complicated due to the lack of resources and interrelated socio-demographic factors which influence pregnancy outcomes with one in four women reportedly drinking alcohol post conception, prior to pregnancy recognition (O'Connor et al., 2011). Further findings suggest that seventy one percent of mothers reportedly stopped drinking at pregnancy recognition, however most were unaware of their pregnancy status until well into their first trimester, a critical period for the damaging effects of prenatal alcohol exposure (Moore & Persuad, 2003; O'Connor et al., 2011). These findings raise important questions about preconception screening for alcohol use and its associated risk factors, which become especially important in low income communities with confounding factors, such as maternal nutrition and lack of effective contraception (Chersich et al., 2012; Urban et al., 2008; Morojele et al., 2009).

While Coles and colleagues (1991) reported that half of the children born to heavy drinkers did not show abnormal features, a review conducted by Abel (1995), estimated 4.3 percent of heavy drinkers, (i.e. those consuming an average of 2 or more drinks per day or 5-6 drinks in one occasion) gave birth to a FAS child. The issue of whether a safe level of prenatal alcohol exposure during pregnancy exists remains controversial. Findings suggest that low to moderate amounts of alcohol (≤ 2drinks/day) during pregnancy was acceptable and did not affect children's behaviour and IQ between 2-14 years of age (Henderson et al., 2007; Robinson et al., 2010). Other research, however, suggests that even small quantities of prenatal alcohol exposure

negatively impacts child behaviour (Larkby & Day, 1997). A 2001 study found children exposed to less than one drink a week were three times more likely to have scores in the delinquent range at 6 to 7 years of age, as measured by the Achenbach Child Behaviour Checklist, (Sood et al., 2001). Children whose mothers consume alcohol are more likely to show signs of general growth delay, with smaller head size and lower birth weights, with links between early physical development and poorer developmental outcomes and lowered IQ's evident (Coles et al., 1992; Mills, Graubard, Harley, Rhoads & Berendes, 1984; Streissguth, Clarren & Jones, 1985). Animal and neuroimaging studies have demonstrated the cognitive, behavioural impairments and developmental delays associated with FAS as being directly related to structural and functional changes within the CNS, often referred to as 'primary disabilities' (Adnams et al., 2001; Coles et al., 1991; Jones & Smith, 1973; Kodituwakku, Kalberg & May, 2001; Mattson et al., 2001; Roussotte et al., 2011; Streissguth et al., 1996; Sulik, 2005; West, 1986). The following section describes some important structural and functional abnormalities associated with prenatal alcohol exposure research.

2.4 Structural and Functional Abnormalities Associated with Prenatal Alcohol Exposure (PAE)

2.4.1 Structural abnormalities.

Prenatal alcohol disrupts the normal growth and passage of neural cells leading to abnormalities within the brain and spinal cord. Two general criteria are associated with structural central nervous system (CNS) abnormalities required for a FASD diagnosis namely; 1) a small head circumference and 2) damage to key regions of the brain (Hoyme et al., 2005). It is well known that head circumference of an infant, regardless of prenatal alcohol exposure, constitutes a simple, inexpensive tool to assess the development of the central nervous system (CNS),

identifying infants at risk of future neurodevelopmental disorders (Garcia-Alix, Saenz-de Pipaon, Martinez, Salas-Hernandez & Quero, 2004). Studies in the eighties showed that alcohol use during pregnancy caused microcephaly, a small head circumference relative to an infant's body size and weight (Ernhart et al., 1985; Rosset et al., 1983). Post-mortem studies of children with heavy prenatal alcohol exposure describe smaller head sizes (below the 10th percentile), with approximately 80% of children with FASD presenting with microcephaly, making it an important criterion for a diagnosis (Clarren, Alvord, Sumi, Streissguth, Smith, 1978; Jones & Smith 1973; Hoyme et al., 2005; Naidoo, Chikte, Laubscher & Lombard, 2005; Mattson & Riley, 1998; O'Leary, 2004; Riley et al., 1995; Urban et al., 2008; Viljoen et al., 2005; Wisniewski, Dambska, Sher & Quzi, 1983). Children whose mothers stopped drinking before the end of the second trimester had larger head circumferences than those whose mothers continued to drink throughout pregnancy, which suggests that pregnant women may avoid additional injury to their unborn child if they stop drinking before the third trimester (Coles et al., 1991). Alcohol related structural changes in specific regions of the brain, may well be attributed to brain size, neurological functions and infant head size. Evidence from both animal and neuroimaging studies indicate that neurological effects of alcohol exposure are not global but affect more vulnerable areas of the brain regions namely; the basal ganglia, corpus callosum, cerebellum and hippocampus (Autti–Ramo & Granstrom, 1991; Archibald et al., 2001; Chandler, Richardson & Gallagher, 1996; Coles, et al., 1997; Goodlet & Horn, 2001; Guerri et al., 2009; Hannigan, Berman, Zajaz, 1993; Hannigan & Berman, 2000; Humphriss, Hall & MacLeod, 2010; Hunt, Jacobson & Torok, 2009; Kalberg et al., 2006; Kodituwakku, 2007; Maier & West, 2001a,b; Mattson et al., 2001; Mattson, Crocker & Nguyen, 2011; Parnell et al., 2009; Riley & McGee,

2005; Roebuck, Mattson & Riley, 1998; Sowell et al., 1996; Sulik, 2005; Valenzuela, Lindquist, Zamudio & Bulcock, 2010; West, 1986; West, Goodlett, Bonthius, Hamre & Marcussen, 1990).

Researchers describe decreased volumes of the basal ganglia related to motor control, cognitive functions; executive functions which include the ability to shift from one task to another and inhibit inappropriate behaviour (Archibald et al. 2001; Cortese et al., 2006; Mattson et al., 1996). Alterations in size and volume of the corpus callosum have been shown to contribute to deficits in attention, intellectual functioning, reading, learning, verbal memory and executive and psychosocial functioning, with some studies suggesting that 7% of children with FAS lack the corpus callosum altogether (Bookstein, Sampson, Streissguth & Connor, 2001; Riley et al., 1995; Swayze et al., 1997). The cerebellum, another particularly vulnerable region of the brain, has been implicated, known to impact movement, including sensorimotor coordination, muscle tone and balance as well as attention, executive functions and other complex tasks (Archibald et al., 2001; Kodituwakku, Segall & Beatty; 2011; Mattson et al, 2001; O'Hare et al., 2009; Salman et al., 2006; Sowell et al., 1996). Research findings differ in the description of the extent of damage to the hippocampus. While some researchers have shown that the size of the hippocampus in the left temporal lobe is smaller than in the right lobe, others have found the size of the hippocampus less affected compared to other brain regions (Archibald, et al., 2001; Riikonen, Salonen, Partanen & Verho, 1999). Behavioural studies have further supported the argument that the hippocampus is damaged due to prenatal alcohol exposure with findings suggesting deficits associated with learning, spatial memory and other memory functions (Mattson et al., 2001; Uecker & Nadal, 1996). The extent of structural damage caused by prenatal alcohol exposure,

inevitably affects later more specific areas of development. The following provides a brief description of the functional implications thereof.

2.4.2 Functional abnormalities.

Infants and children with FASD show enormous individual variability in ages at which specific developmental, cognitive milestones and levels of achievement are reached. In order to meet the FAS diagnostic criteria, an individual must have either global deficits (<25th percentile) or deficits in specific functional domains, with global cognitive deficits defined as a decreased IQ (≤ 3 standard deviations below the mean) or a presence of significant developmental delay amongst younger children (Paton & Croom, 2010). While some level of cognitive deficit characterizes individuals with FASD most do not have mental retardation, with findings indicating IQ functioning with scores between 65-82 (Conry, 1990; Jones et al., 1973; Lemoine et al., 1968; Mattson & Riley, 1998). In a study describing the longitudinal development of alcohol exposed infants to adolescents, Streissguth and colleagues (1994) describe that the FAS individuals fell into the borderline mental retardation range with a mean IQ of 79. For individuals not meeting the FAS criteria, but exposed to prenatal alcohol, an average IQ of 90 was reported. Further studies have shown that an IQ or developmental score in the low average to average range does not rule out the presence of neurocognitive deficits or mental health problems (Streissguth, Randels & Smith, 1991). When faced with everyday learning, the majority of children diagnosed with FAS, experience varying degrees of difficulties in the moderate to severe range of cognitive performance. While global delays are not always apparent amongst alcohol exposed children, most children tend to display specific developmental deficits in functional domains (Goldschmidt, Richardson, Stoffer, Geva & Day, 1996). Variations in average IQ's over the numerous studies are likely to arise from differences in severity of

diagnosis, age at testing and exclusions resulting from the type of IQ tests used. Specific developmental domains, as assessed by the GMDS/ER and deficits associated with prenatal alcohol exposure are presented in detail in section 2.7. Furthermore, it is likely that atypical brain development in children with prenatal alcohol exposure is further moderated by genetic factors and the quality of postnatal experience, described in section 2.8.

2.5 Epidemiology of FASD

Precise figures regarding FAS are difficult to obtain, however, it seems likely that most attempts are underestimates due to misdiagnoses with other disorders, including those of attention deficit hyperactivity disorder (ADHD), autism, major depressive disorder, bipolar disorder, oppositional disorder and conduct disorder (Burd et al., 2003; Chudley, Kilgour, Cranston & Edwards, 2007; O'Connor et al., 2002). In reviewing international prevalence rates of FAS, the United States describe rates of between 0.5 and 2.0 per 1,000 births (May & Gossage, 2001). In Australia, FAS rates of 0.02 per 1,000 have been reported, with 2.76 per 1,000 amongst Aboriginal children (Elliot & Bower, 2004). South Africa has amongst the highest reported FAS rates worldwide, with levels of between 40.5 to 119.4 per 1000 in various South African communities (Chersich et al., 2012, May et al., 2007; Viljoen et al., 2005; Urban et al., 2008). While May and Gossage (2001) suggest that the type of research design and method used to determine prevalence may influence reported rates, later research indicates time itself may create differences between reported rates, possibly due to awareness (Chersich et al., 2012; May et al., 2005). Using data from numerous studies, researchers have provided a guide for estimating the rate of all measureable effects of prenatal alcohol exposure, where it is thought that FAS, ARBD and ARND may affect as many as 10 per 1,000 births (1%) (Abel, 1995).

2.6 Risk factors associated with prenatal alcohol exposure (PAE).

In reviewing available international and local studies, certain maternal factors have been shown to be linked to an increased risk of having a child with FAS, these include; maternal age at pregnancy, gravidity (number of previous pregnancies), parity (number of previous births), low socio-economic status, unemployment, use of tobacco and other drugs (Abel, 1995; May et al., 2005, 2008; Odendaal, Steyn, Elliot & Burd, 2009; Urban et al., 2008; Viljoen et al., 2002). Epidemiological studies conducted in South Africa, Italy and the United States describe mothers of children with FASD as smaller than controls in the same country in height, weight and body mass index (BMI) (May et al., 2005; Urban et al., 2008; Viljoen et al., 2002). While studies conducted in small, rural towns of South Africa have revealed major nutritional deficiencies amongst all participants, mothers with FASD children show significantly lower intake of riboflavin, calcium and DPA (an omega 3 fatty acid) , with zinc and B vitamins likely playing a role (May et al., 2004; Tamura et al., 2004). May et al. (2005) report significantly smaller head circumference measurements of mothers with children diagnosed as FAS, which may suggest some mothers have FAS or PFAS themselves. Age of drinking onset, length of time mothers had been drinking, quantities consumed and frequency and timing of use during pregnancy have been shown to further impact the severity of prenatal alcohol damage (Abel, 1998; Hoyme et al., 2005; Jacobson, Jacobson & Sokol, 1994; May et al, 2007; 2008; Stratton et al., 1996; Sulik, 2005; Urban et al., 2008; Viljoen et al., 2005). Findings suggest it is not the total amount of alcohol consumed, but the number of drinks consumed on one occasion, peaking blood alcohol content (BAC) levels, which negatively affects the developing fetus (Abel, 1998; Khaole et al., 2004; Livy, Miller, Maier & West, 2003; Maier & West, 2001a,b; Pierce & West, 1986; West & Goodlett, 1990). High risk pregnant mothers regularly partake in binge like drinking patterns,

consuming an average of 2 or more drinks per day or 5-6 units in one occasion, which peaks BAC levels increasing structural, behavioural and cognitive risks to their inborn child (Maier & West, 2001a,b; May & Gossage, 2001; Caley, Kramer & Robinson, 2005). Studies conducted on children aged 7 years of age in South Africa revealed mothers of children with FASD drank more alcohol, more frequently, in a heavier episodic fashion than comparison mothers with non FASD children (May et al., 2005).

Few studies have examined the psychological characteristics associated with risky drinking amongst women with FASD diagnosed children. Those that have describe women in these circumstances as often suffering from low self-esteem, with varying degrees of depression and are likely to have partners who typically engage in similar, heavy drinking patterns (Abel, 1998; Chetty, 2012; Flynn & Chermack, 2008; May et al., 2005, 2008; Stratton et al., 1996; Viljoen et al., 2002; Wilsnack, Klassen, Schur & Wilsnack, 1991). While some risk factors cannot be modified, such as maternal genotype for alcohol dehydrogenase shown to influence alcohol intake, alcohol metabolism, fetal effects and ethnicity, others such as poverty and low socio economic differences, often associated with prenatal alcohol exposure, are further influenced by poor nutrition, paternal stress, genetics and social factors (Goodlet, Gilliam, Nichols & West, 1989; Streissguth & Dehaene, 1993; Warren., et al., 2001). Since socio-economic deprivation itself may lead to developmental delays over specific domains, it is critical that the development of prenatal alcohol exposed children from low socio-economic circumstances (typical environments alcohol affected children are found) are compared to healthy children from the same environment (Coles, 1995).

The history of alcohol consumption, amongst indigenous people in South Africa has a long, history. During colonial times, alcohol was exchanged for labour and goods a practice known as, 'the dop system' which only recently was abolished on wine farms in the Western and Northern Cape (Parry, 2005). Further factors changing the patterns of alcohol consumption include, urbanisation, changes in gender and age roles, and intense mass marketing and promotion of alcoholic beverages (Parry, 2000). Considered a middle income country, South Africa is characterized by high levels of poverty and inequality, with conditions of adversity, disproportionately affecting the mixed coloured and black/african ethnicities (O'Connor et al., 2011). Most studies on neuropsychological deficits of individuals with FASD have focused on children and adolescents, making direct longitudinal comparisons to this study difficult with researchers recognizing that earlier studies during infancy would better enable preventative measures. With the highest reported international rates of FASD, surely South Africa has an ethical obligation to understand the exact developmental nature of the disorder and in so doing prevent and manage later secondary disabilities which place unnecessary burdens on already over extended communities.

Considering its impact on early childhood development, the study of FASD is of considerable relevance to all professionals in school settings, administrators, school psychologists, policy makers and researchers, especially from areas with known high rates of alcohol use. The lack of specialized medical, psychiatric and/ or psychological services in most impoverished communities in South Africa impacts early identification, thereby influencing subsequent intervention. The following section provides a description of the main childhood developmental domains, with reference to their developmental theories and the impact of prenatal alcohol exposure and key socio-demographic factors on early developmental performance.

2.7 Childhood Development

Child development is a process, encompassing biological and psychological changes from infancy through to adolescence (Shonkoff & Phillips, 2000). Developmental progressions over various domains include motor skills (e.g., sitting, running, and more complex movements, etc.), language skills (both expressive and receptive), cognitive, executive function/self-regulatory skills (e.g., symbolic thought, memory, and logic) and social-emotional skills (e.g., a sense of self, empathy and how to interact with others) (Kuhn & Siegler, 1998). While for assessment purposes, developmental abilities are usually divided into domains, typically they overlap often influencing each other with later stages of development succeeding earlier ones, which according to Piaget (1952; 1963), ultimately prove more adaptive to the demands of the environment. It is imperative, that when assessing a child's mental development, a full investigation of motor, social and cognitive abilities is undertaken (Bondurant-Utz & Luciano, 1994; Griffiths, 1954; Meisels, 1996; Nuttal, Romero & Kalesnik, 1992). Seen as a process rather than a product, developmental theorists agree that changes are sequential and usually progressive in nature involving increasing complexity, embedded within a particular environmental context.

With roots in both the mechanistic and organismic perspectives, Piaget's theory describes development as being based on 1) maturation (the process through which biological change takes place accounting for neurological changes through physical growth); 2) experience (the interaction with the environment); 3) social transmission (the process when information, attitudes and customs are transmitted from one group to another, e.g. parent to child), and 4) equilibrium (the internal motivational system and demands of the environment) (Piaget, 1952; 1963). In agreement with Piaget, Griffiths (1954; 1970) refers to development as the individual progression at which the growth and maturation of a child's attributes and abilities takes place.

McCall (1981) proposed the concept of canalization, in which during the first 18-24 months developmental function is largely maturational, with individual, unstable differences less associated with either genetic or environmental factors. The following section provides a description of each developmental domain as assessed by the GMDS/ER with reference to relevant developmental theories, and the impact of prenatal alcohol exposure and socio-demographic factors on their developmental outcome.

2.7.1 Motor skills.

Defined as the development of abilities essential to movement and acquisition of motor skills, the advancement of motor ability forms an important component of a child's general development (Knoesen, 2005). For infants and young children, large motor skills include the progression of learning to walk and run, walking on a line, controlling movements and jumping with age, while fine motor skills, such as picking up an object, holding eating utensils, drawing and writing, all involve eye-hand coordination and muscle control (Gallahue & Ozmann, 1995; Griffiths, 1954; 1970; 1986; Matney, 1999). Attainment of both gross and fine motor skills is significant, with children gaining new ways of exploring their environment. Piaget's (1963) highly regarded theory of cognitive development proposes four stages to intellectual development, revisited under cognitive skill development in section 2.7.2, namely; 1) sensorimotor thought (0-2years); 2) pre-operational thought (2-7years); 3) concrete-operational thought (7-11years) and 4) formal operational (11 years and older). While each stage is described in Table 2 particular reference is given to the sensorimotor and pre-operational stages in text, with participants in the current study aged between 7 months and 5 years.

Table 2

Piaget's Four Stages of Cognitive Development

Stage	Description	Age Range
Sensorimotor	Infant progresses from reflexive, instinctual action at birth to the beginning of symbolic thought. Infant constructs an understanding of the world by coordinating sensory experiences with physical actions.	Birth to 2 years
Preoperational	Child begins to represent the world with words and images; which reflect increased symbolic thinking, beyond the connection of sensory information and physical action.	2 to 7 years
Concrete Operational	Child now can reason logically about concrete events, classifying objects into different sets (schemas).	7 to 11 years
Formal Operational	More abstract and logical reasoning by adolescents. With more idealistic thinking.	11 to 15 years

Note. Adapted from Santrock, J.W. (2002). *Life span development*

According to Piaget's theory of cognitive development during the sensorimotor stage (0-2years of age), an infant's knowledge is limited to his sensory perceptions and motor activities, with behaviours limited to simple motor responses usually caused by sensory stimuli (Piaget, 1963). To make sense of their environment and develop basic representations from which later more cognitive schemas are derived, children at this stage utilize innate behaviour patterns to ascertain the relationship between sensations and motor behaviour. While cognitive functioning at the beginning of this stage is limited to involuntary reflex actions without rational thought or

representation, drastic changes, due to maturation give rise to later more symbolic, complex cognitive abilities. While the order of each stage is the same between children, the pace at which children proceed through the stages may vary, especially in regard to children exposed to prenatal alcohol (Piaget, 1963; Bjorklund & Bjorklund, 1992). Research confirms early motor skills contribute to later developmental achievement with difficulties in motor skills often indicative of the presence of neurological or perceptual problems (Bushnell & Boudreau, 1993, Luiz et al., 2004).

While findings differ about the extent of delay on early motor development associated with prenatal alcohol exposure, evidence from both animal and human studies indicate both gross and fine motor functions are vulnerable to the effects of prenatal alcohol exposure (Autti-Ramo & Granstrom, 1991; Barr, Streissguth, Darby & Sampson, 1990; Chandler et al., 1996; Connor, Sampson, Streissguth, Bookstein & Barr, 2006; Conry, 1990; Jacobson et al., 1993; Jones & Smith, 1975; Kalberg et al., 2006, Mattson & Riley, 1998; Roebuck, Simmons, Richardson, Mattson & Riley, 1998; Valenzuela et al., 2010; Van der Leeden et al., 2001). Infants with FAS tend to suffer from tremors, show a difficulty in responding to sensory stimuli and display a weak suckle (Martin, Martin, Sigman & Radow, 1977). These early delays amongst toddlers and young children compound with findings presenting later delays associated with; motor milestones, weak grasps, difficulty in writing or drawing, being clumsy, balance problems, poor dexterity (Connor, et al., 2006; Conry, 1990; Mattson et al., 2010, Mattson et al., 1998, Roebuck et al., 1998). Despite difficulties associated with balance, older children with prenatal alcohol exposure typically do not display deficits in gross motor behaviours such as running and jumping (Adnams et al., 2001, Chandler et al., 1996).

The link between motor and mental ability is evident with findings suggesting that when basic developmental functions, often motor, are compromised by prenatal alcohol exposure, socio-demographic factors or both, they impact on the development of subsequent higher-order skills (Herbert, Eckerman, Standton, 2003; Salman et al, 2006). Gusella and Fried (1984) describe how prenatal alcohol exposure reportedly affects the mental scale of the Bayley Scales of Development more than the motor scale amongst infants aged 13 months. Their findings concur with earlier studies reporting decreased mental and motor scores amongst heavily exposed infants, assessed at 8 months of age using the Bayley Scale of Infant Development (Streissguth, Barr, Martin & Herman, 1980). Other researchers failed to find any relationship between prenatal alcohol exposure and gross motor ability (Adnams et al., 2001; Richardson & Day, 1991). No significant group motor effects were reported by Adnams and colleagues (2001) on the Locomotor scale of GMDS of 34 South African children, diagnosed with FAS aged 7 years of age, when compared to a matched control group of healthy children. Although some gross and fine motor deficits, associated with prenatal alcohol exposure, may diminish with practice, reports suggest, later decreases over more complex, fine motor and higher-order cognitive skills become more evident with age, which generally persist into adulthood (Adnams et al., 2001; Connor, Sampson, Bookstein, Barr & Streissguth, 2000; Jacobson et al., 1993; Kable & Coles, 2004; Kalberg et al., 2006; Kartin, Grant, Streissguth, Sampson & Ernst., 2002; Kodituwakku et al., 2001; Mattson, Goodman, Caine, Delis & Riley, 1999; Mattson & Riley, 1998; Osborn, Harris & Weinberg, 1993; Stanton & Goodlet, 1998; Stratton et al., 1996; Willford, Richardson, Leech & Day, 2004).

Childhood development is multi-factorial, drawing on biological, socio-economical and cognitive aspects, all of which work together to determine a child's developmental potential.

Regardless of prenatal alcohol exposure, studies suggest that socio-demographic factors may similarly contribute to motor delays (Cockcroft et al., 2008; Gale et al., 2006; Giagazoglou, Kyparos, Fotiadou & Angelopoulo, 2007; Hack et al., 1995; Richards et al., 2002; Shenkin et al, 2004; Silva, Metha, O'Callaghan, 2006). In one such study conducted on 40 South African black infants, aged between 13 to 16 months, maternal education was found to be positively associated with gross motor development of infants. The study found that children of a low socio-economic status performed significantly poorer than those from more affluent homes (Cockcroft et al., 2008). Similar motor delays were reported in a Greek study using the GMDS/ER to investigate the relationship between maternal education and residential area on infant development of 800 children aged between 37 and 72 months (Giagazoglou et al., 2007). While their findings described better fine motor ability associated with children from urban areas those from rural areas performed significantly better in terms of gross motor ability. While differences may be attributed to variations between urban and rural living conditions in Greece, it provides evidence for the role of socio-demographic factors on motor development during childhood.

2.7.2 Cognitive skills.

Analytical skills, mental problem-solving, visual perception, memory, early mathematical abilities and language all encompass cognitive developmental skills (Griffiths, 1970; 1986; Huntley, 1996). For, infants and toddlers, early cognitive development involves problem-solving with objects, such as learning to stack or nest objects, and an early understanding of math, demonstrated by sorting objects and basic mathematical knowledge (Griffiths, 1954, 1986; Kuhn & Siegler, 1998). As children approach school-going age, cognitive development broadens to include early knowledge of numbers, addition and subtraction, and familiarity with letters and print (Schneider & Bjorklund, 1998). The preoperational stage, of Piaget's cognitive

development theory, described in Table 2, between the ages of two and seven occurs when the child begins to characterise the world through words and images, beyond basic sensory information and physical action, reflecting an increase in symbolic thought, usually associated with increased language development (Piaget, 1952, 1963). Assimilation and accommodation are important processes which make this possible. With assimilation, children match concepts arising from their environmental interactions with previously formed mental schemes. Accommodation entails the modification of these existing schemes based on the environmental interaction. Both provide a state of equilibrium, a balance between the individual and the environment. By providing opportunities for children to expand the schemas they are learning about, cognitive development is further stimulated. As children develop, single schemas become more complex ones, building on one another, with an opportunity for revisiting earlier schemas, not fully mastered (Athey, 1990).

Evidence from studies of children exposed to prenatal alcohol describes significant impairment in problem-solving abilities, abstract thinking, planning and cognitive flexibility (Adnams et al., 2001; Coles et al., 1992; Kodituwakku et al., 2001; Mattson et al., 1999; Mattson & Riley, 1998; Streissguth et al., 1994). Research on memory has shown specific problems in the encoding of information (i.e. the learning of new material) with exposed children more likely to retain new information when encouraged, using more trials or different teaching methods (Coles et al., 1997; Coles, Lynch, Kable, Johnson & Goldstein, 2010; Kaemingk, Mulvaney & Halverstan, 2003; Kerns, Don, Mateer & Streissguth, 1997; Mattson et al., 1996; Mattson & Roebuck, 2002; Mattson et al., 1998; Roebuck-Spencer & Mattson, 2004). Converging findings suggest that children with FASD process information more slowly, perform worse than controls on tasks

involving interhemispheric transfer of information and show decreased processing with more demanding higher-order tasks requiring greater cognitive effort (Burden, Jacobson & Jacobson, 2005; Burden, Jacobson, Sokol & Jacobson, 2005; Jacobson et al., 1994; Roebuck, Mattson & Riley, 2002). Consistent with previously described delays in information processing recent findings describe alcohol exposed children to be slower with visual processing than controls in letter recognition with children with FASD generally, performing worse, than their typically developing counterparts, over specific cognitive functions as task complexity increases (Kodituwakku et al, 2011). Greater difficulty with math than with reading and spelling has been reported amongst studies of children heavily exposed to prenatal alcohol (Olson et al., 1998; Howell, Lynch, Platzman, Smith & Coles., 2006). Findings from a prospective study conducted by Goldschmidt and colleagues (1996) indicate the linear-dose response association of prenatal alcohol exposure during the second trimester on mathematical skills, with higher exposed children performing worse. Executive functions refer to specific higher-order cognitive skills involved in planning, sequencing, and appropriate use of feedback in response selection, set shifting, cognitive flexibility, ability to inhibit, concept formation and reasoning (Morris, 1996). While the roots of children's executive functioning are apparent in infancy, it is only during early childhood, as the frontal lobe develops, that executive functions advance (Anderson, 1998). Both clinical with longitudinal studies indicating prenatal alcohol exposure affects executive functioning, likely caused by the structural, damage to the developing brain during pregnancy (Coles et al., 1997; Kerns et al., 1997; Kodituwakku, Handmaker, Cutler, Weathersby & Handmaker, 1995; Kodituwakku et al., 2001; Rasmussen, 2005). Problems associated with executive functioning amongst alcohol-exposed infants have been identified as early as 3 months of age with alcohol-exposed infants showing greater difficulty in maintaining and manipulating

three items of information simultaneous, compared to non-exposed subjects (Jacobson et al., 1993). Using several neurodevelopmental tasks tapping active executive functions amongst school-going children, Kodituwakku and colleagues (1995) maintain that delays associated with executive functions form the basis for most cognitive impairment described amongst individuals with FAS, with deficits associated with academic and later functioning, dysfunctions in behaviours and daily functioning (Bishop & Gahagan & Lord, 2007; Kelly, Day & Streissguth, 2000; Kodituwakku et al., 2001; Rasmussen, Wyper & Talwar, 2009; Schonfield, Paley, Frankel & O'Connor, 2006; Steinhausen, 1995; Streissguth et al., 1991; Thomas, Kelly, Mattson, Riley, 1998; Whaley, O'Connor & Gunderson, 2001; Rasmussen, et al., 2009). Studies have indicated that individuals with a FAS diagnosis demonstrate similar executive functioning deficits as those exposed to some levels of alcohol, with both groups performing worse than controls (Kodituwakku et al., 1995; Kodituwakku et al., 2001; Mattson et al., 1999). Kodituwakku et al. (2001) describe the predictive relationship between neuropsychological measures of executive functioning and behavioural problems in alcohol-exposed children. Behavioural and emotional issues associated with prenatal alcohol exposure and typical childhood developments are further described in section 2.7.4.

While Piaget believes cognition is primarily based on biological determinants intrinsic to the child, Vygotskian thinking postulates that cognitive abilities are formed and built up in part by interactions with the social environment (Vygotsky, 1978; 1986). Researchers describe the complex interplay of biological factors (genes, brain growth and neuromuscular maturation) and environmental influences (parent-child relationships, community characteristics, cultural norms) on early childhood development (Gottlieb, 1991; Pollitt, 2000; Shonkoff & Phillips, 2000).

Negative effects of socio-economic status on children's school readiness in the US are believed to be mediated by attention processes, suggesting that low quality, environments affect cognitive development in part by decreasing children's abilities to attend (NICHD, 2003). Increasingly, research demonstrates that cognitive abilities may be as strongly affected by the quality of the environment as they are by genetics (Shonkoff & Phillips, 2000). The cognitive, social and emotional development of children is generally promoted by caregivers who are responsive and interacting than compared to those from less stimulating homes (Shonkoff & Phillips, 2000).

While little is known of the epigenetic influences of cognitive abilities, it seems likely that their impact may prove more important than conditions of poverty, malnutrition and ill health. Twin study findings suggest the importance of genetic influences, which contribute to approximately half of the variance in cognitive abilities (Kovas, Haworth, Dale & Plomin, 2007). Regardless of the factors associated with cognitive development, it becomes evident that language parallels higher-order development, not only forming an important part of overall cognition but offers an essential, early indicator of a child's overall development.

2.7.3 Language skills.

Long before the emergence of the first word, language development begins (Bloom, 1998). Critical for socialisation and academic success, language skills allow for the understanding of directions and the ability to be able to communicate thoughts and feelings to others. Early indicators during infancy include babbling, pointing and gesturing, with first words and sentences emerging in the first two years leading to the rapid expansion of words between ages 2 and 3 years (Woodward & Markman, 1998). Overall, literature suggests children with FASD exhibit impairments in areas such as word articulation, naming ability, word comprehension and both receptive and expressive language skills comprehension (Abkarian, 1992; Becker et al.,

1990; Carney & Chermak, 1991, Church et al., 1990; Conry, 1990; Fried & Watkinson, 1988; 1990; Fried, O'Connell & Watkinson, 1992; Janzen et al., 1995; Mattson & Riley, 1998; Mattson et al., 1998; McGee et al., 2009).

Developmental theories, disagree on the roots of language development, with no one theory adequately explaining learning and language development in the first three years. According to Skinner (1957) language is learnt through reinforcement, with children imitating what they see and hear in exploring their environment while in contrast, Chomsky (1959) believed that speech is acquired by maturation, in much the same way as basic motor skills. Perhaps the most holistic viewpoint is that of Piaget (1963) who saw language development as being an example of symbolic behaviour, dependent on the child's interaction with the environment. Table 3 summarises key language milestones.

Investigations into the language skills of children with prenatal alcohol exposure have produced inconsistent results, likely due to variations between studies in methodologies, subject characteristics and task characteristics, with fewer still cohort studies examining the relationship between PAE and delayed language development in preschool children (Abel & Hannigan, 1995; Carney & Chermack, 1991; Church et al., 1997; Conry, 1990; Fried & Watkinson, 1988; 1990; Greene, Ernhart, Ager, Sokol, Martier & Boyd, 1991; Greene, Ernhart, Martier, Sokol & Ager, 1990; Janzen et l., 1995; Kaplan-Estrin, Jacobson & Jacobson, 1999; Kodituwakku et al, 2011; Mattson et al., 1998; O'Leary, Zubrick, Taylor, Dixon, Bower, 2009).

Table 3

Early Language Milestones

Age of Child	Typical Language Development
6 months	• Vocalization with intonation • Responds to his name
12 months	• Uses one or more words with meaning • Understands simple instructions, especially if vocal or physical cues are given
24 months	• Can name a number of objects • Combines words into a short sentence • Responds to such commands as "show me your eyes (nose, mouth, hair)"
36 months	• Use pronouns I, you, me correctly • Handles three word sentences easily • Should be able to give his sex, name, age
48 months	• Names common objects in picture books or magazines • Knows one or more colours • Can repeat 4 digits when they are given slowly • Can usually repeat words of four syllables
60 months	• Can use many descriptive words spontaneously • Knows common opposites • Can count to ten • Should be able to repeat sentences as long as nine words • Should be able to define common objects in terms of use (hat, shoe, chair) • Should know his age

Source. Adapted from Molteno, (1991). Psychomotor Development, in *Child Health for All: A Manual For Southern Africa*

Overall, literature suggests children with FASD exhibit impairments in areas such as word articulation, naming ability, word comprehension and both receptive and expressive language skills comprehension (Abkarian, 1992; Becker et al., 1990; Carney & Chermak, 1991, Church et al., 1990; Conry, 1990; Fried & Watkinson, 1988; 1990; Fried, O'Connell & Watkinson, 1992; Janzen et al., 1995; Mattson & Riley, 1998; Mattson et al., 1998; McGee et al., 2009).

Results amongst younger children are more variable with Greene et al. (1990) describing no significant receptive or expressive language impairments in exposed children aged between 1-3 years of age. In contrast, Fried and Watkinson (1988; 1990) found reduced language comprehension at 13 months, 2 and 3 years but failed to find language deficits in the same cohort at ages 4, 5 or 6 years. Similar associations were reported by Coles et al. (1991) who failed to find any association between alcohol exposure and the language ability of a group of children aged 5 years 10 months. Younger children tend to show global deficits, while older children display deficits in specific areas, such as syntax and pragmatics or social communication with effective social communication requiring complex cognitive skills (Abkarian, 1992; Carney & Chermack, 1991; Coggins, Timler & Olswany, 2007; Shaywitz, Caparulo & Hodgsons, 1981). The link between language and cognitive development is well known demonstrating that impairments in language impairments often exhibit deficits in non-linguistic cognitive domains including those associated with executive functions (Arvedson, 2002, Johnson, Im-Bolter, Pascual-Leone, 2003, Schul, Stiles, Wulfeck & Townsend, 2004). The development of language, regardless of prenatal alcohol exposure, provides important evidence of central nervous system (CNS) veracity and remains an important milestone for children, as well as a good indicator of overall development (Coplan et al., 1998). Considered as the most cognitive of the GMDS-ER

subscales, language acquisition has the highest correlation with intelligence, indicative of overall cognitive development (May et al., 2007). Lags in vocabulary growth may be indicative of less infant directed speech, suggesting the impact of home environments (Hart & Risley, 1995). Studies in the United States have shown children from low income families develop slower vocabularies and speak fewer words than their higher income counterparts by preschool (Hart & Risley, 1995). Not only is language development important in the overall cognitive development but it forms an integral part of emotional and social development, linguistic and social skills continuously being developed as children interact with their environments (Piaget, 1952; Bowlby, 2000; Vygotsky, 1978; 1986; Bronfenbremmer, 1979; Bronfenbrenner & Ceci, 1994).

2.7.4 Social/emotional skills.

Social development is comprised of socialization, where we are deliberately taught and trained by parents and others about how to fit in and function in society, which occurs with or without formal schooling, as we learn about our culture by observing others (Segall, Dasen, Berry & Poortinga, 1999). Traditionally, Personal-Social development was seen as falling outside of the scope of the intelligence construct, yet researchers have since realized that social development is important in forming an integral part of a child's general development, with direct and profound effects on other developmental domains (Parker & Asher,1987; Saami, Mumme & Campos, 1998). Assessments of child development, especially during the pre-school period, are now strongly urged to consider personal-social development (Griffiths, 1970; Nuttall et al., 1992). Benner (1992) maintains aspects of this domain of development are multifaceted, including, the development of attachment, the growth of self, the emergence of emotions, and the development of adaptive behaviours which includes self-care. Through socialising with others, we begin to understand our thoughts, feelings, adaptability and temperament. While Erikson's theory of the

stages of psychosocial development provides an adequate description of psychosocial development, its focus lies on the development of personality as a function thereof, describing the impact of social experience across the whole lifespan. Table 4 highlights Erickson's stages, which apply to children, in the sample, from birth to 5 years of age.

According to Erikson's theory, healthy adjustment to various phases occurs with the child able to solve basic conflicts in a positive manner (Erikson, 1982; Tomlinson-Keasey, 1985). Often characteristic of children with FASD, children are unable to discern the thoughts and feelings of others are more likely to behave aggressively. Warm, responsive relationships with caregivers prove essential for teaching children to trust, and for acquiring early strategies for dealing with frustration, fear and other negative emotions, (Bowlby, 2000; Thompson & Raikes, 2006).

Bowlby argued that as the child becomes more autonomous, the quality of emotional attachment of the parent regulates the child's willingness to explore, returning to the mother as a base, as he or she discovers the surroundings. A secure attachment relationship is thought to lead the child into a range of psychologically healthy developmental pathways. Vygotsky's influential learning theory proposes that children learn actively and through hands-on experiences, suggesting that higher order functions originate as actual relationships between individuals with parents, caregivers, peers and the culture (Vygotsky, 1978).

Table 4

Erikson's Epigenetic Sequence of Psychosocial Development

Stage of Childhood	Psychosocial Outcome	Social Achievement and Consequence	
Infancy (birth to 11 years) : Oral–sensory	Trust versus Mistrust	Mutuality of interests, attachments	Withdrawal, Depression
Toddlerhood (2-3 years): Muscular-anal	Autonomy versus shame and doubt, in which the issue is whether the child can feel independent of others	Self-control, Personal esteem	Failure, dependence
Childhood (4-5 years): Locomotor-genital	Initiative and responsibility versus guilty functioning, in Which the issue is whether, the child can feel competent and be active	Adventure; participation	Seclusiveness

Source. Adapted from Newman and Newman (1987). Development through life: A psychosocial approach. Chicago, IL: Dorsey Press.

Increased evidence supports the notion that FAS or PAE affected individuals experience a wide range of deficits in adaptive skills and problem behaviours (Burd et al., 2003; Mattson & Riley, 2000; Steinhausen, 1995). Infants with FAS show signs of hyperactivity to sensory stimuli, irritability, self-soothing problems, general hyperactivity and attachment difficulties (Coles et al., 1991; O'Leary, 2004). Young children with FAS tend to be impulsive, uninhibited, intrusive, insensitive to social cues, lacking in social judgement, overly friendly and excessively demanding affection and physical contact (Green, 2007; Mattson et al., 2001). Hyperactivity and

attention problems are amongst the most frequently reported symptoms associated with prenatal alcohol exposure with literature suggesting links between FASD and attention deficit hyperactivity disorder (Kodituwakku et al., 1995, Mattson & Riley, 2000, Coles et al., 1997; Kodikuwakku et al., 2006; Nanson & Hiscock, 1990). Children with FASD often lack social judgment and show poor attentional functions making learning from consequence difficult which make learning from consequence difficulty (Abkarian, 1992; Kodikuwakku et al., 1995; Kodikuwakku et al., 2006; Olson et al., 1998). Adolescents and adults with FAS frequently display poor communication and socialisation skills, such as poor judgement, difficulty perceiving social cues, overly demanding of attention, stubbornness, bragging, and an inability to respect personal boundaries for their age (Mattson et al., 2001). However, reports suggest differences in neurocognitive and behavioural characteristics between children with FAS and PAE and those with a primary diagnosis of ADHD (Coles et al., 1997). Further differences in adaptive skills have been noted, with alcohol-affected children demonstrating an arrest in development of adaptive ability and more likely to exhibit antisocial behaviours, show a lack consideration for others and resist limits and requests by authoritarian figures (Carmichael-Olson et al., 1997; Crocker, Vaurio, Riley & Mattson, 2009; Roebuck et al., 1999; Thomas et al., 1998; Whaley et al., 2001). In a study based on the parental responses of adolescents with FASD significant socialization domain problems were identified in particular, those of the failure to consider consequences of one's actions, the lack of responsiveness to social cues and poor interpersonal relationships (Streissguth et al., 1991). These difficulties in socialisation make interacting with others and their environments difficult, forcing children and adults to internalise feelings, which in turn may manifest as low self-esteem, social isolation and mood disorders (Bronfenbrenner., 1979; Bronfenbrenner & Ceci, 1994; Burd et al., 2003; O'Connor et al., 2002).

While it is clear that heavy prenatal alcohol exposure causes structural damage affecting functional abilities and specific domains, developmental delays are likely confounded by various biological disadvantages, which children carry with them from birth, causing a cumulative impact on early childhood (Breitmayer & Ramey, 1986; Rutter, 1979; Sameroff, Seifer, Baldwin & Baldwin, 1993). Studies in early childhood development emphasise the importance of considering relevant covariates in their effects on childhood development (Engle et al., 2007; Neuspiel, 1994; Viljoen et al., 2002, 2005). The following section briefly describes the cumulative effects of some key socio-demographic factors which may further exacerbate delays associated with early childhood development, over the domains, discussed in this section.

2.8 Cumulative Risk Factors Associated With Early Childhood Delays

Developmental outcomes are influenced by a number of biological, social and family risk factors (Breitmayer & Raemy, 1986; Bronfenbremmer, 1979; Bronfenbrenner & Ceci, 1994; Rutter, 1979; Sameroff et al., 1993). The developing child is seen by Bronfenbremmer, in his theory of ecological development (1979), as being at the centre of a set of interconnected systems impacting directly or indirectly. According to the ecological theory as shown in Figure 1 if relationships in the immediate microsystem, i.e. family, mother and/or father, break down, the quality of the child's ability to explore other parts of his environment decreases. Children looking for the affirmations that should be present from the child/parent (or child/caregiver) relationship, look for attention in inappropriate places with deficiencies often presenting as anti-social behaviour, lack of self-discipline, and inability to provide self-direction, especially in adolescence (Addison, 1992). Similar behaviours are reported amongst children with prenatal alcohol exposure, as described earlier in section 2.4 (Abkarian, 1992; Carmichael-Olson et al., 1997; Kodikuwakku et al., 1995; Roebuck et al., 1999). For optimum growth and development

children need a loving and secure environment. While physical needs are being met their emotional and psychological needs also have to be fulfilled. Love, care, attention and guidance allow children to develop into stable, well-adjusted and sociable adults. Healthy mother-child interactions are seen as being essential in developing stable and loving relationships. Based on the love and affection received by infants from their mothers they learn to trust. They grow by watching, imitating and being guided by her (Bowlby, 2000; Klein, 2001; Rye, 2001). Children in an orphanage from a study conducted in Iran (Hunt, 1983, cited in WHO, 1997) show no interest in social interaction. In general, these children showed a lack of normal development in language, social and emotional skills. When these children were compared to a group receiving early stimulation and social enrichment, the difference of 3 standard deviations in IQ between groups is striking (Hunt, 1983). While all adults have the capacity to love and guide children under their care external factors may further inhibit their ability to do so effectively, such as poverty, stress of daily living, ill health, depression, addictions or other emotional problems. While the current study did not include mother-child interactions as a variable it is important to reflect on the link between it and the quality of parenting amongst children with parents consuming large amounts of alcohol. This study contributes to the effects of the "nature" view in the age old "nature/nurture" debate.

The question Bronfenbrenner's ecological model poses is, given that development continues on a specified path, how does the world, surrounding the child help or hinder their developmental course? As the child develops both physically and cognitively, the interaction between systems becomes more complex further influenced by confounding variables. Adverse developmental outcomes of children living in poverty are likely due to the cumulative effects of exposure to

increasing numbers of risk factors, becoming more apparent with age (Glascoe, 2001; Laughton et al., 2010; Rydz, Shevell, Madjnemer & Oskoui; 2005).

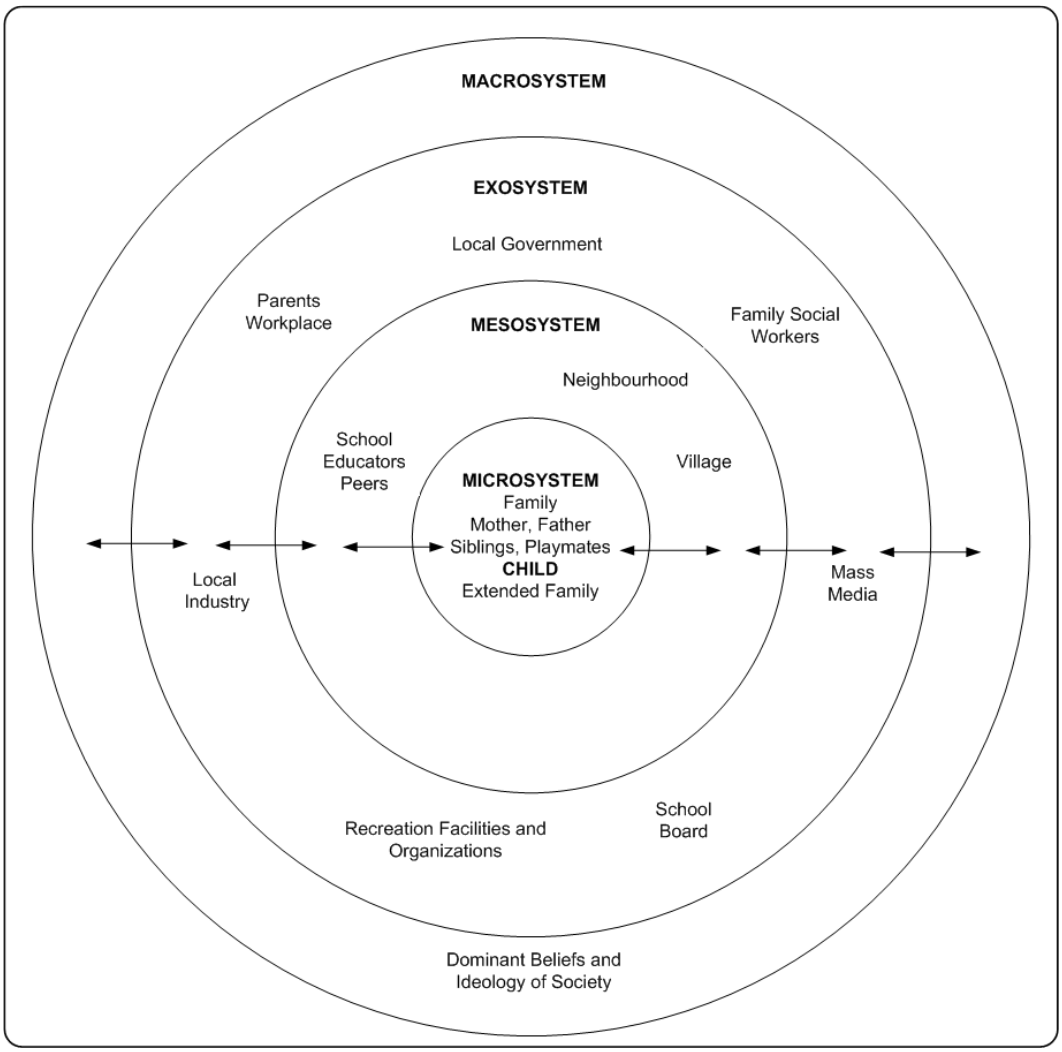


Figure 1. Bronfenbrenner's Ecological Model of Child Development

From an ecological viewpoint, developmental delay and FASD are both often the end result of a complex interaction between diverse social, political, environmental and genetic risks. Some risk factors associated with FASD, for example, cannot be changed, such as the mother's maternal

genotype for alcohol metabolism and ethnicity (Stoler, Ryan & Holmes, 2002). In other words, more cumulative risks are related to poorer cognitive development, psychological distress and behaviour problems and development of communication and symbolic behaviour (Hooper, Burchinal, Roberts, Sameroff et al., 1993; Sameroff, Seifer, Barocas, Zax & Greenspan, 1987).

Studies concur that when examining prenatal alcohol exposure, it is important to consider relevant covariates, with findings describing how risk factors often co-occur and interfere with children's development (Baker–Henningham et al., 2003; Bradley & Corwyn, 2002; Engle et al., 2007; Hamadani & Grantham–McGregor, 2004; Hussong, Huang, Curran, Chassin & Zucker, 2010; Neuspiel, 1994; Viljoen et al., 2002, 2005). The cyclical nature of prenatal alcohol exposure, biological risk factors and adverse postnatal environment exacerbate each other further contributing to generalised and/or specific atypical central nervous system development. While attention has been placed on the impact of prenatal alcohol exposure on developmental abilities, in section 2.7 Figure 2 serves to place biological risk factors and adverse environmental environment into context in understanding their cumulative effect on early childhood development.

Adverse postnatal environments strongly influence elementary and more specific developmental functions, with research further suggesting the impact of other confounding factors such as; maternal nutrition, poor maternal education, increased maternal stress and depression, larger family sizes and general lack of stimulation (Baker–Henningham et al., 2003; Bradley & Corwyn, 2002; Brooks–Gunn & Duncan, 1997; Brooks-Gunn, Klebanov & Duncan 1996; Brooks-Gunn, Guo & Furstenberg, 1993; Chetty, 2012; Cockcroft et al., 2008; Ensminger &

Fothergill, 2003; Gale et al., 2006; Grantham–McGregor, et al., 2007; Hack et al., 1995; Hamadani & Grantham–McGregor, 2004; Kirksey et al., 1994; Lalloo, 1997; Mistry, Biesanz, Taylor, Burchinal & Cox, 2004; Richards et al., 2002; Shenkin et al., 2004; Short, 1987; Silva et al., 2006; Sirin, 2005).

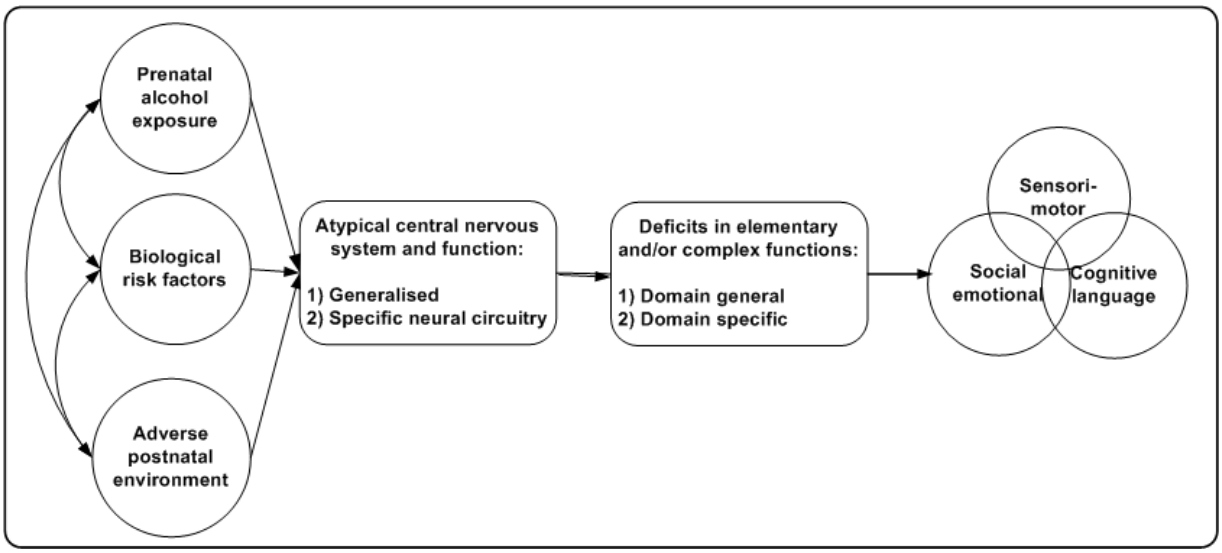


Figure 2. Pathways connecting cumulative risk factors and poor child development
Adapted from (Elliot & Bower, 2004; Kodituwakku et al, 2011 & Walker et al., 2007)

While prenatal alcohol exposure is likely a contributing factor to poor overall development, research has shown that gender and ethnic differences further impact early developmental ability over various domains (Bygren, Kaati & Edunsson, 2001; Herman, Acosta & Chang., 2008; Kapil et al., 2007; Mick et al., 2002; Pembrey et al., 2006; Rasmussen, Horne & Witol, 2006; Weinberg, 1992). The tendency to conceptualise the results of gender based research findings within the context of verbal, quantitative, and visual-spatial abilities has been heavily criticised (Halpern, 1997; Naglieri & Rojahn, 2001). Evidence suggests that specific areas of the male and

female brain, rather than developmental abilities associated with language, spatial memory, motor coordination and social adaptive functioning, may differ in their rate of development (Hanlon, Thatcher & Cline, 1999). A pattern of differences is clearly evident, indicating that boys are better at certain tasks and skills, such as spatial tasks and mathematical problem solving, whereas girls do better in terms of verbal fluency, writing ability and perceptual speed (Arcenaux, Cheramie & Smith, 1996; Born, Bleichrodt & Van Der Vlier, 1987; Blakemore, Berenbaum & Liben, 2009; Halpern, 2000; Maccoby & Jacklin, 1974). While previous findings during infancy suggest no motor ability differences based on gender, variations emerge after 2 years (Blakemore et al., 2009; Mondschein, Adolph & Tamis-LeMonda, 2000). Girls perform better than boys in terms of fine motor abilities, with boys outperforming girls on tasks related to muscular strength, such as ball throwing and distance (Karapetsas & Vlachos, 1997; Pollatou, Karadimou & Gerodimos, 2005; Thomas & French, 1985). These differences may have more to do with physical skill, than developmental ability. Earlier research focusing on language development suggests that while girls generally learn to talk slightly earlier than boys, these differences were not statistical significant (Maccoby & Jacklin, 1974). More recent studies have found that girls between the ages of 2 and 6 years are slightly ahead of boys in terms of most language measures, particularly that of vocabulary growth (Berglund, Eriksson & Westerlund, 2005; Fenson et al., 1994; Galsworthy, Dionne, Dale & Plomin, 2000; Morriset, Barnard & Booth, 1995; Rome-Flanders & Cronk, 1995). While these findings indicate advancements in girl's language development during early childhood, boys eventually catch up (Blakemore et al., 2009). Girls also tend to have fewer speech disorders, such as stuttering and dyslexia, than boys (Halpern, 2000; Hyde & McKinley, 1997).

Some differences have been found by researchers in visual-spatial ability as early as the infant years. According to Reinisch and Sanders (1992), females have a perceptual advantage during early infancy, with fluency differences emerging from 2 years. In a study reviewing literature on gender differences amongst pre-schoolers, Levine, Huttenlocher, Taylor and Langrock (1999) describe pre-school boys as being more accurate than girls at spatial tasks that measure accuracy of spatial transformations scoring higher on the Mazes subtest of the Wechsler Pre-school and Primary Scale of Intelligence. They concluded that gender differences in favour of boys are present on spatial tasks by age 4 years 5 months, with similar findings reported by Halpern (1993). In summary, boys are more advanced in spatial and motor skills than girls while girls were found to be more advanced over cognitive, fine motor and language ability than boys (Edwards, 1975; Kruger, 1983; Townes, Trupin & Fay, 1980).

Studies reporting associations between lower birth weight or head circumference at birth and poorer developmental performance have mainly focused on "high-risk" individuals (born of low birth weight, premature or intrauterine growth restriction (IUGR) (Hack et al., 1995; Bhutta, Cleves, Casey, Cradock & Anand, 2002). Research conducted in developing countries further suggest decreased infant birth anthropometrics are likely associated with poor maternal nutrition influencing central nervous system development and later functional development in adulthood (Brown & Pollitt, 1996; Fattal–Valevski et al., 1999; Grantham–McGregor & Fernald, 1997). In a study conducted in South India on healthy children aged 9-10 years of age born full term, findings suggest birth weight and head circumference at birth were positively associated with two tests of cognitive function measuring learning, long term storage, retrieval and visual-spatial ability, after controlling for potential confounders (Veena et al., 2010). Several previous studies

describe similar positive associations between birth weight and/or head circumference and subsequent cognitive abilities (Brennan, Funk, Frothingham, 1985; Gale et al., 2006; Silva et al., 2006). While evidence suggests that small head circumference is associated with decreased cognitive abilities, size may have more to do with the prenatal environment or genetic factors, unless prenatal alcohol exposure is evident.

Strong correlations exist between passive smoking and lower birth weight, with research describing associations between smoking, drinking and increased risk of preterm labour, low birth weight and growth restrictions (Odendaal et al., 2009; Rubin, Craig, Gavin & Suner, 1986). Earlier animal studies have similarly shown associations between paternal alcohol use and low birth weight, with later cognitive and behavioural delays (Cicero, 1994; Hegedus, Alterman & Tarter, 1984; Little & Sing, 1987).

Research conducted on breastfeeding has been shown to reduce infant morbidity and develop closer mother-infant relations, with breastfed children from developing countries showing higher language abilities and improved motor abilities associated with duration of exclusive breastfeeding (Anderson, Johnstone & Remley, 1999; Beaver et al., 2010; Daniels & Adair, 2005; Dewey, Cohen, Brown, Rivera, 2001; Grantham–McGregor, Fernald & Sethuraman, 1999; Jacobson & Jacobson, 1999; Jain et al., 2002; Kramer et al., 2008; Tozzi et al., 2012; Uauy & Andraca, 1995; Uauy & Peirano, 1999). Studies from developing countries further confirm improved motor abilities associated with duration of exclusive breastfeeding.

Prenatal alcohol exposure causes devastating structural and functional abnormalities, associated with elementary or more specific cognitive and/or developmental deficits. While maternal

alcohol consumption and biological risk factors determine the extent of prenatal alcohol exposure, various socio-demographic factors, often themselves associated with heavy prenatal alcohol use compound already vulnerable communities, initiating the effects of cumulative risk factors on early childhood development. The following chapter provides an overview of the methods used in the current study, with reference to the study's aims and objectives, research questions, sampling procedure and assessments used.

Chapter 3 - Method

3.1 Introduction

Literature reviewed in the previous chapter indicated that the majority of research studies investigating the effects of prenatal alcohol exposure tend to be cross-sectional in nature with a focus on either the cognitive or behavioural deficits typically measured during middle childhood. To augment the paucity of developmental research there is a need for long-term developmental profiles of infants exposed to varying degrees of prenatal alcohol, using an instrument which assesses development over various developmental domains. Despite both the original and revised Griffiths Scales being used for a number of theoretical and clinical research studies on South African communities, to our knowledge no studies have used both versions to assess and compare development of young children over time, with known prenatal alcohol exposure.

This chapter presents the primary and specific aims of this research. It further defines the research methods used, namely the study design, sampling methods and instruments employed to collect the data. Finally, consideration is given to the research procedure and the data analyses used to answer the studies research questions.

3.2 Research Aims and Questions

The primary aim, from which secondary aims and research questions were derived, was to describe and compare the longitudinal developmental relationships between three groups of children during early childhood, with varying degrees of prenatal alcohol exposure from an impoverished community of South Africa.

Secondary aims sought to compare performance on the subscales and General Quotients (GQ) within each of the three groups over the two time periods, while a third aimed to investigate the relationship between infant developmental performance and later achievement at 5 years, over the GMDS/R subscales and General Quotient (GQ). Finally, the relationship between socio-demographic factors on the developmental performance within each of the three groups, during infancy and at 5 years of age, was investigated, which formed the fourth aim.

From these study aims, the following research questions were formulated, which guided the investigative process of the study. Statistical analyses used to answer the research questions are briefly described in section 3.8, with statistical findings further presented in detail in Chapter 5.

3.2.1 Research question 1.

What early childhood developmental differences exist between 3 groups, namely; FAS/PFAS, PAE and Non-exposed, over a period of 5 years?

Since it is well known that excessive prenatal alcohol exposure has a negative impact on child development, it was hypothesized that the FAS/PFAS group would perform significantly poorly,

at both time points, over all developmental domains relative to the Control group. Research suggests that moderate prenatal alcohol exposure may be just as detrimental, therefore it was hypothesized that the PAE group would similarly perform significantly poorly over all developmental domains, at both time points, relative to the control group.

Research has shown that children with heavy prenatal alcohol exposure continue to present with developmental delay over specific domains over time, it was hypothesized that findings within the FAS/PFAS group would suggest significantly poor performance when compared to the Control group (Streissguth et al., 1994). Since little research exists regarding the impact of moderate prenatal alcohol exposure on childhood development over time, a priori hypothesis within group comparison was not made.

3.2.2 Research question 2.

What is the relationship between infant developmental performance over subscales, measured by the Infant version of the GMDS (Time 1) and achievement at 5 years of age (Time 2) measured by the Child Version GMDS/ER?

Since the GMDS/R was used to assess development at Time 1 and Time 2 albeit using different scale versions (Infant & Revised-Child) it was hypothesized that developmental performance at Time 1 on each developmental domain would be significantly correlated with the same domain at Time 2 for each group. While the constructs being measured for each domain would differ due to the developmental abilities of children at the two time points, it was expected that infants who performed poorly at Time 1 would continue to perform poorly into early childhood.

3.2.3 Research question 3.

Which socio-demographic variables are associated with developmental achievement at infancy and 5 years of age?

Given that research has shown the impact of environmental variables on developmental delay and considering the characteristics of the sample included in the present study, it was hypothesized that the developmental performance of all three groups, over specific domains, would be influenced by specific demographic and socio-economic variables at both time points. It was further assumed that the groups with structural damage due to prenatal alcohol exposure would perform worse over more developmental domains when performance was correlated with demographic and /or socio-economic variables.

3.3 Research Design

Having expanded the research topic, into the noted aims and questions, the research design serves to describe the practical progress of the study. In the context of the present research study a descriptive design was used to provide information regarding prenatal alcohol exposure further describing socio-demographic variables and conditions from a South African perspective. Since no variables were experimentally manipulated or controlled for, the design was considered non-experimental, while an opportunity to define terms and clarify existing concepts provided for a more exploratory approach (Rosnow & Rosenthal, 1996). While flexible, the descriptive, exploratory nature of the design is typically unstructured proving difficult in explaining manipulations and measurements between variables (Knoesen, 2003). To strengthen the generalisability of findings, to which findings are valid and conclusions are sound, the longitudinal approach of the study further attempts to draw comparisons and identify causal relationships between variables, by following participants over time conducting repeated

observations (Jackson, 1995; Louw & Edwards, 1997). While this longitudinal approach adds to the generalisability of the study, further increasing its validity, reliability and minimizing personal bias, it falls short on providing a 'human' element of behaviour, attitude and perception. The inability of a qualitative method to investigate causality and the use of the questionnaire and developmental measures used to collect the numeral data of the study further motivates the quantitative approach. The following section provides details of the study sample, and the sampling procedures used.

3.4 Background to Sample

Participants were drawn from the town of De Aar, predominantly a sheep farming area in the Upper Karoo region of the Northern Cape which historically, offered the largest railway junction in South Africa. However, towards the end of the last century, operations were significantly reduced resulting in exceptionally high unemployment rates and complex social circumstances contributing to increased levels of alcohol abuse in the communities.

Although a democratic society since 1994, in many communities, the structural and personal changes have yet to reach the majority of South African people at a grass roots level, with many living in conditions similar to those of the 'apartheid' era with changes made in the educational, social and financial spheres less obvious. In impoverished communities, structural adversities, such as political oppression and poverty or interpersonal hardships like accidents or illness remain prevalent with interpersonal troubles stemming from the larger structural adversities (Greenop, 2004). An example of this may be alcoholism, often exaggerated by structural stresses such as unemployment.

Studies exploring early childhood development have shown the impact of the child's environment, on overall biological, cognitive, psychological and physical development (Barbarin & Khomo, 1997; Barbarin & Richter, 2001) especially those associated with socio-economic markers. Previous studies, describe delays associated with early childhood development as being confounded by poverty, nutrition and maternal health (Baker–Henningham, et al., 2003; Bradley & Corwyn, 2002; Engle et al., 2007; Hamadani & Grantham–McGregor, 2004; Hussong et al., 2010; Neuspiel, 1994; Viljoen et al., 2002, 2005), while recent South African findings suggest socio-demographic variables such as the level of maternal education, maternal depression, high parity and previous loss of a child further contribute to overall developmental performance during early childhood (Cockcroft et al., 2008; Chetty, 2012). However, less is known as to which early childhood developmental domains are affected by which socio-economic factors and to what degree these are influenced by prenatal alcohol exposure during early childhood development. It is imperative that all studies dealing with the vulnerable aspect of early childhood development therefore consider these socio-demographic factors. This study seeks to understand these nuances while including the often ignored aspect of prenatal alcohol exposure. The following describes the sampling procedure utilised in the study.

3.5 Sampling procedure

The sampling procedure provides an imperative part of a research study adding to its overall validity. Researchers, generally, prefer probabilistic or random sampling methods as they prove more accurate and rigorous. However, due to the specific clinical characteristics associated in making a FAS/PFAS diagnosis, and the difficulty in identifying these individuals from a poorly resourced community, especially during infancy, a combination of purposive and convenience sampling was used in the current study (Kotras, 1998; Singleton et al., 1988).

Of the 500 recorded births in De Aar between 2002 and 2003, 392 families consented and completed both a clinical and developmental assessment at Time 1. Motivated by the central limit theorem, the maximum possible number of child and mother dyads was considered necessary to increase the sampling distribution to normality (Howell, 2002). In other words sample sizes of 30 or more show that "sample mean" distributions tend to approach normality. With the likelihood of some of the other investigated, independent variables being normally distributed, the probability of subsequent parametric statistical examinations was thereby increased (Murphy & Davidshofer, 2001). Figure 3 illustrates the sampling procedure, including details of the recruitment and attrition of participants. Of the 394 participants at Time 1, 135 completed their clinical and developmental assessments at Time 2 (5 years). Sample attrition was expected, due to the longitudinal nature of the study and may further be explained by geographical mobility, infant/mother mortality, incomplete evaluations and assessments between time points and inconclusive maternal information. Due to logistical constraints, the sample was further reduced between Time 1 and Time 2 with healthy participants, not meeting the diagnostic criteria at Time 1, not invited back for follow-up at Time 2 (n=247). While one hundred and thirty five participants returned at Time 2 for clinical and developmental evaluations, only 121 had completed a full maternal interview, forming the final study sample. Inclusion in the current study was based on full completion of the clinical examination and neurodevelopmental assessment at both Time 1 and Time 2 as well as the completion of a maternal interview (n=121).

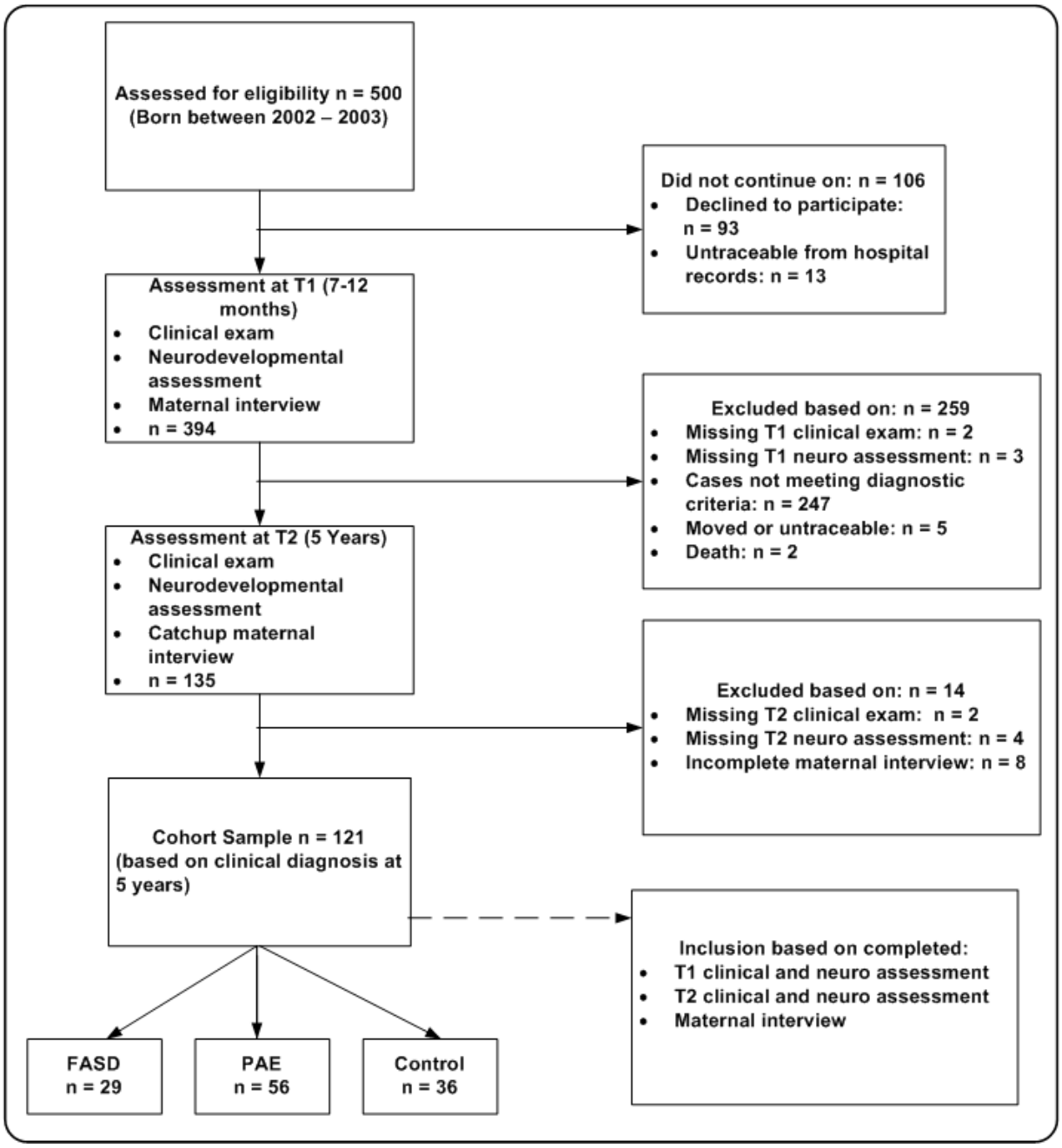


Figure 3. Recruitment and attrition of participants for the study

While participants were assigned a clinical diagnosis at Time 1 (7-12months), clinical features at 5 years, considered definitively more accurate, was used to classify participants into one of three

groups. Forty one children were assigned to the FAS/PFAS group, 44 to the PAE group and the remaining 36 to the Control group. The relatively small sample size, typical in this kind of research, may be explained partly by the longitudinal nature of the study as well as the stringent, diagnostic criteria related to FAS/PFAS, especially amongst an infant sample (Cockcroft et al 2008; Schuler, Nair & Harrington, 2003). A limitation associated with a smaller sample size is that of an increased standard error, limiting the representative nature of the findings from the sample, while influencing the distributions (Field, 2009). In other words, because not all participants from the community have an equal chance of being part of this study sample, findings cannot be considered representative of general early childhood development within the community. However, the longitudinal attribute of the study adds to its statistical power, providing an important description of developmental profiles amongst young children specifically with prenatal alcohol exposure.

For purposes of investigating the research aims and questions, three measures were used to collect the necessary data from maternal-child dyads. Each measure is discussed below and where applicable details regarding the psychometric properties and evidence of cultural validity and reliability are included. While the order of the measures presented below reflects their sequence of administration, they were not all completed on the same day.

3.6 Assessments

3.6.1 Clinical diagnostic evaluation.

As detailed in Chapter 2, commonly, four clinical diagnostic schemas exist, all retaining the three key diagnostic features of; prenatal/postnatal growth deficiency; characteristic pattern of facial anomalies and evidence of CNS dysfunction (Astley & Clarren, 2000; Bertrand et al.,

2005; Chudley et al., 2005; Hoyme et al., 2005; Jones & Smith, 1975). Differences between criteria have been related to the number of facial characteristics considered necessary to definitively obtain the FAS diagnosis (Riley, Infante & Warren, 2011). Well established and reliable, the Hoyme-Revised IOM criteria were used by specialist clinicians with dysmorphology training at Times 1 and 2 (Hoyme et al., 2005; IOM, 1996; Stratton et al., 1996). In order to meet a FAS diagnosis, participants who had ≥2 of the characteristic facial features; short palpebral fissures (<10^{th} percentile), thin vermillion border (rank 4 or 5), smooth philtrum (rank 4 or 5); evidence of growth retardation; where height and weight ≤10^{th} percentile and evidence of CNS involvement; where head circumference (OFC) ≤10^{th} percentile or structural brain abnormality, were assigned to the FAS group. Those with at least two of the three characteristic FAS facial features and evidence of growth retardation of either; height or weight (≤10^{th} percentile) or head circumference (≤10^{th} percentile) or an abnormal neurocognitive assessment, received a Partial FAS (PFAS) diagnosis (Hoyme et al., 2005). While according to the Hoyme et al. (2005) criteria, a FAS/PFAS diagnosis may be considered clinically distinctive, even in the absence of a history of maternal alcohol consumption in pregnancy. Maternal alcohol use during pregnancy, in the current study was obtained from the maternal interview with all children in the FAS/PFAS group, with a confirmed alcohol exposure during pregnancy. Participants with either a clinical FAS or PFAS diagnosis were assigned to the FAS/PFAS group (Hoyme et al., 2005).

While the Hoyme et al., (2005) schema provide criteria regarding Alcohol Related Birth Defects (ARBD) and Alcohol Related Neurodevelopmental Disorder (ARND), these subtler neurological features, with particular reference to ARND, prove harder to detect during infancy. Participants whose mothers acknowledged drinking prior to and/or during pregnancy but lacked sufficient

clinical evidence of the typical FAS/PFAS features, were assigned to a Prenatal Alcohol Exposure (PAE) group, deemed appropriate in representing those with possible ARBD, ARND. Finally, those with no evidence of FAS/PFAS features and a confirmed history of no to low (<7units alcohol per week prior to pregnancy recognition) exposure prior to the pregnancy, were assigned to the Control group. Anthropometric information related to birth measurements, such as birth weight, length and head circumference was obtained by the clinician during the examination, from the Road to Health birth card.

3.6.2 The infant and extended versions of the Griffiths Mental Developmental Scales (GMDS/ER).

The predictable and sequential nature of child development leads to the use of an instrument that identifies behaviours typical to age appropriate levels of development (Lidz, 2003). One of the most widely used assessment tools; the GMDS/ER focuses on both cognitive and physical development across early childhood from birth to 8 years of age and has been considered an objective developmental rather than intellectual test (Breakwall et al., 2006). Identifying both specific areas as well as overall development is essential when assessing early childhood development. Researchers agree that when assessing a child's mental development, a full investigation of motor, social and cognitive abilities should be undertaken (Bondurant-Utz & Luciano, 1994; Meisels, 1996; Nuttal et al., 1992).

Originally developed in 1954 by Ruth Griffiths, the GMDS were the first published scales designed to assess infant and child development in the following skills areas of; Locomotor, Personal–Social, Language, Eye and Hand Co-ordination, Performance and Practical Reasoning

(included from ages 2-8years) (Griffiths, 1954;1984). Due to the longitudinal nature of the current study, both the infant and child scale sets of the GMDS/ER were used. The revised version of the GMDS/ER was used on the older child set at their second assessment, and were unavailable for the infant scale set, where the original version was used (2006 revision). The following section provides a brief description of each subscale forming the GMDS/ER. Original validation research on the Griffiths Scales, conducted in the 1960's, yielded a positive and moderately high correlation between each subscale and the General Quotient (GQ) with Griffiths (1970) suggesting that this correlation indicated a common factor of general intelligence in each subscale. The following provides a description of each subscale, assessed by the GMDS/ER.

The **Locomotor Subscale** assesses gross motor skills such as balance, co-ordination and the control of movements. Physical strength, skill in speed and rhythm are further measured. The scale measures the series of developing skills that result in the achievement of an upright posture leading on to learning to walk, run and climb. Items include age appropriate tasks such as sitting, walking unaided, kicking a ball and hopping on one foot. While locomotor development tends to mirror general development in young children, low correlations have been described with later cognitive achievement (Luiz et al., 2004).

The **Personal-Social Subscale** measures the child's level of independence, self-help skills, co-operation in play and general socialising skills. This scale is often influenced by emotional factors with both the overprotected and neglected children usually performing poorly on this subscale (Griffiths, 1984). Age appropriate items include the child's ability to dress and undress,

fastening buttons, and efficacy at the table. Through a friendly interaction with the child further information such as child's age, surname and number of friends at school can be obtained. Most of this information is based on questions posed either to the children themselves, if they are old enough, or accompanying mothers/caregivers influencing the subjective nature of this subscale. A number of questions within this scale, are language based, therefore it is important to take this subscale into account when interpreting results of the Language subscale.

The **Language Subscale** is the most intellectual of the subscales which assesses both the child's receptive and expressive language use and skills. Poor performance may not necessarily indicate low intellectual functioning, but may be explained by partial or complete hearing loss, lack of stimulation or mixed language families (Kotras, 1998; 2003). Auditory memory and the child's understanding of similarities and differences are considered in this scale. Age appropriate items include the number of words used, naming and identifying of objects and colours, understanding the meaning of words, providing differences and similarities and being able to comprehend situations. In the GMDS-ER, this subscale is known as the Language subscale, while in the Infant Version it is referred to as the Hearing and Language subscale (Kotras, 1998; 2003; Luiz et al., 2004). For purposes of consistency, it is referred to as the Language subscale.

The **Eye and Hand Co-ordination Subscale** involves an assessment of the child's fine motor skills, manual dexterity and visual perceptual skills, necessary for many school related tasks. Co-ordination, persistence and care for work are also measured while information regarding perception of space and form- relations can also be obtained (Kotras, 1998; 2003). The age

appropriate items which form this scale involve tasks such as drawing, threading beads and cutting with scissors.

The **Performance Subscale** assesses the child's manipulation skills, work speed and precision while including that of visual spatial skills. The scale is measured through the completion of tasks such as building towers and bridges out of blocks, form boards and timed, pattern completion tasks. The previous Eye-Hand Co-Ordination and Performance subscales require demonstration of the child's ability to carry out fine motor tasks.

The **Practical Reasoning Subscale** only introduced to children over the age of 2 years, assesses the ability to solve practical problems, understand basic mathematical concepts about moral and sequential issues. Age appropriate items include counting, questions relating to height, weight and length or knowledge of the days of the week. Attention and the ability to concentrate play a major role in assessing the child's performance on this subscale as well as the other five subscales (Luiz et al., 2004b; Sweeny, 1994). This subscale involves the assumption of the cognitive maturation of a sufficient level of general cognitive abilities and skills, therefore a poor performance on this subscale, if associated with a low score on the Performance subscale, may indicate a developmental delay/learning difficulty (Luiz et al., 2004). In addition, the Practical Reasoning subscale includes a lot of language based items, and children with speech and language delays may perform poorly on this subscale.

Administration and scoring procedures as described in the original and revised analysis manuals were followed (Griffiths, 1954, 1984; Luiz et al., 2004). Items of both the GMDS and-ER are arranged in sequential order of difficulty for each age group (Luiz et al., 2006; Stewart, 2005) with the scale content changing with age. Thus, although the subscales assessed between versions do not change, with the exception of the addition of the Practical Reasoning subscale for the 2-8 year old scale, items being tested on each subscale vary, according to age and developmental abilities (Allan et al., 2002).

Test items were administered, starting 4 months below the child's chronological age with the first six consecutive items passed considered the basal score, while six consecutive failed items formed the ceiling score (Bhamjee, 1991; Griffiths, 1984). Incidentally, items failed below the basal or passed above the ceiling were not penalised or credited (Luiz et al., 2006).While the general quotient (GQ) is a composite of all subscale scores, each scale can also be used alone, with consensus means ranging between 99.79 and 100.46, with standard deviation scores from 0.58 to 17.43 (Adnams et al., 2001). In other words, a standard score of 100 in any subscale, would place the child's performance within the average range, whereas a score below 70 (<2standard deviations) would indicate a significant degree of developmental delay or learning disability in that subscale (Luiz et al., 2004). Due to the unavailability of South African norms for the GMDS and-ER versions, and given the socio-economic and educational differences between the South African and United Kingdom samples, it would be inappropriate to compare standardised norms. Furthermore, the use of two versions of the GMDS and-ER at different points in time, with differing means and standard deviations, required that scores be presented in equal units, therefore *z* scores were calculated (Ivens & Martin, 2002). Raw scores for both the

infant and the childhood versions for each of the GMDS/ER subscales and the summed general quotient (GQ) corrected for prematurity at Time 1 were converted to individual *z*–scores, where the raw score minus the mean score, is divided by the standard deviation (Field, 2009). Z-scores expressed in terms of standard deviations from their means, resulted in these *z*-scores having a standardised distribution with a mean of 0 and a standard deviation of 1. Owing to the absence of population means and standard deviations for the South African population of the GMDS/ER, scores were calculated from the study sample as a whole. With norm scores of the GMDS/ER ranging between 50 and 150 for each scale, scores less than 50 were assigned the lowest nominal value of 50 to reflect a score of <-3 SD below the mean for statistical purposes. Deviations of an individual's standardised *z*- score from that of the normative mean were used to classify developmental impairment or delay over specific subscales, scores ≤-2 SD indicated significant developmental delay while those ≥-2 indicated no delay (Field, 2009).

Although various research studies have made use of the GMDS/ER over many different populations in South Africa, showing good test-retest reliability, as well as the ability to predict long term development, no South African standardisation exists yet (Allan, 1988, 1992; Bhamjee, 1991; Cockcroft et al., 2008, Heimes, 1983; Kotras, 2001, Lombard 1989; Luiz et al., 2006; Mothuloe, 1990; Stewart, 1997). South African studies have contributed to restructuring the items on the revised editions making them non-threatening and reasonably culturally fair with some cultural developmental differences reported which may be influenced by external variables, such as socio-economic status and levels of maternal education (Cockcroft, et al., 2008; Houston-McMillan, 1988). The usefulness of a test score strongly depends on its validity and reliability. The GMDS-ER provides particularly favourable reliability findings, with the

alpha coefficient reaching 0.993, with recent studies on content and construct–related evidence further proving it a valid diagnostic developmental test (Luiz et al., 2006).

Most participants did not speak English and where necessary verbal instructions and items were translated into Afrikaans and Xhosa using the back translation method (Allan, 1988; Tukula, 1996). It was felt that this method of translation was acceptable as it had been used for previous translations of the GMDS/ER and as no measures were being adapted or substituted, the mere translation of the instructions was acceptable (Luiz et al., 2004). Full translations of the GMDS/ER were not necessary. As administrators were not fluent in Xhosa, every effort was taken to include a Xhosa translator during the GMDS/ER assessments. However, in cases where this was not possible, mothers/caregivers were conferred with regarding issuing of verbal instruction to the child and interpreting the child's verbal response.

3.6.3 The maternal interview.

A structured questionnaire, piloted on the local population, was completed with mothers by trained interviewers eliciting demographic information and maternal lifestyle variables, such as occurrence and amount of maternal drinking, smoking and use of other drugs (May et al, 2005, 2007; Urban et al 2008;Viljoen et al., 2001). Shorter, proxy interviews were conducted with the primary caregiver, in cases where the mother was deceased or untraceable. This resulted in missing maternal data from some interviews, which impacted the choice of statistical analyses.

A history of maternal alcohol consumption was obtained from mothers using a timeline follow-back method, which has shown to be a reliable and valid method for collecting data on drinking (Sobell et al., 2001, Viljoen et al., 2005). Comparing alcohol consumption and drinking patterns internationally is complicated with questions of how researchers can best conduct comparative

alcohol research. Typically, the 'amount' of alcohol contained in alcoholic beverages varies considerably, with reference to the amount expressed as the percentage of alcohol by volume (ABV) (Foster & Marriot, 2006). A value of 'units' is ascribed to alcoholic drinks, which relates to the amount of alcohol they contain. Variations in the amount of alcohol in a standard drink vary between countries, complicating comparative research studies, while further confusing the media about suggested guidelines. In South Africa, one standard unit equates to approximately 12 g (or 10 ml) of pure alcohol (Wolmarans, Langenhoven & Faber, 1993). Based on the amount of pure alcohol present in alcoholic drinks, researchers typically enquire about the number of 'drinks', 'bottles', 'cans' and /or 'glasses' rather than the grams of alcohol (Bloomfield, Stockwell, Gmel & Rehn, 2003). In an attempt to provide comparative findings, drinks were considered using the following, previously used, standard ethanol units: 340 ml can/bottle of beer (5% ethanol), 120 ml of wine (11% ethanol),95 ml of wine (13.5% ethanol), or 44 ml of distilled spirits (43% ethanol) (May et al., 2008). Photographs of standard beer and wine containers sold locally were shown to participants, to assist with quantification of units, frequency and pattern of drinking.

The following categories were used to determine alcohol usage for group allocation; No-to-low alcohol usage (No or <7 units per week); Moderately High Usage (8-25 units per week); High Usage (26 -≥ 36 units per week).

3.7 Procedure

This study forms part of a larger cohort study conducted by the Foundation for Alcohol Related Research (FARR) in 2003 with clearance from the Committee for Research on Human Subjects (refer to Appendix A1, protocol Number; M01-11-20). Further ethical clearance (refer to

Appendix A2, protocol number; M09-02-22) was awarded to the current study, for follow-up of infants at 5 years of age with the completion of an amended maternal questionnaire.

Permission was obtained from the Department of Health (refer to Appendix A3) to access birth records of all infants born in the public hospital between 2002 and 2003 (*n*=500). In addition, mothers of potential participants living in the town (many women in surrounding rural areas deliver in De Aar and then return home thereafter) were visited by community workers and invited to participate. The process of the study and its voluntary nature was clarified with interested mothers/ caregivers, both verbally and in the form of an information sheet with appropriate opportunities for withdrawal without prejudice, at any time of the study.

Families willing to participate completed the necessary consent forms (refer to Appendices B & C). All parents/guardians of children who had consented to the Time 1 phase at 7-12 months of age were invited to participate in the follow-up, Time 2 study at 5 years of age, with active case follow-up (due to the purposive nature of the sampling procedure) of families with diagnostic concerns. The nature of the study therefore, afforded two sample sets of data namely; developmental data from the children, tracked from infancy through to 5 years of age and data obtained from mothers or caregivers through the maternal interview. Demographic details of the composition of both the child and maternal data sets of the study sample are presented in detail in Chapter 4.

Appointments, held at the Joan Wertheim Centre in De Aar, were set up with consenting families during a week when the clinical team, comprising of a clinician and two of three trained Griffiths

administrators, were in De Aar. Participants were subjected to a clinical diagnostic examination conducted by a specialist clinician with dysmorphology training at both Time 1 (7-12 months) and Time 2 (5 years). Developmental assessments at Time 1 (7-12 months) and Time 2 (5 years) were conducted by the candidate and 2 trained Griffith's administrators all of whom held masters degrees and were formally trained in the administration of the GMDS/ER scales. Consistent, administrative and scoring procedures were followed according to the GMDS and GMDS/ER analysis manuals (Griffiths, 1954; 1984 Huntley, 1996; Luiz et al., 2006). The GMDS/ER assessments took approximately 90 minutes and, as permitted by the GMDS procedure, parents/ caregivers were included in the testing process in an attempt to decrease the child's anxiety. Self-report questions were requested from parents and/caregivers as part of the Personal-Social subscale for both versions of the GMDS/ER, providing a comprehensive overview of the child's development.

Preferably, the maternal interview was completed by the same GMDS administrator, after the completion of the GMDS/ER assessment. However, mothers unavailable at the time of the developmental assessment were interviewed by two community health assistants, trained on the administration of the interview. Both community workers had worked for the Foundation for Alcohol related Research (FARR) during the larger retrospective study and held key counselling skills with valuable knowledge of FASD and a sensitivity to alcohol perceptions held by the community in which they lived. The maternal interview took approximately 45 min to complete. Psychological emotions often associated with a confirmed FAS/PFAS diagnosis, such as maternal guilt or spousal blame, were addressed through counselling after a confirmed diagnosis was made to families and/or individuals.

A case conference where clinical, developmental and maternal information was presented was held where a final FAS/PFAS diagnosis was awarded. If as a result of the study, any clinical, developmental and educational or welfare areas of concern arose, families were referred to the relevant professionals to address the problem areas. Mothers with alcohol dependence were linked with specialist programmes run through local non-governmental organisations. Families of children with a confirmed FAS/PFAS or PAE diagnosis received verbal feedback from both clinicians and psychologists regarding the clinical and developmental symptoms of prenatal alcohol exposure. Families of children who displayed developmental delay on the subscales or the general quotient (GQ) of the GMDS/ER received verbal discussion of the results with the compilation of a report. The psychologist who conducted the assessment spent time with families discussing future expectations of the diagnosed child, with the opportunity to ask any further clinical and/or psychological questions. Follow-up support of families from the study was conducted by the local occupational therapist based at the Joan Wertheim Centre.

All identifying information was removed prior to analysis and kept separate for the sole purpose of feedback to families. A study number was assigned to each participating child and mother dyad, minimising bias, while maintaining overall confidentiality. All other data collected was coded according to the study number and entered, by the researcher, into a standardised, electronic Microsoft Access form. Hard copies of all consent forms, clinical evaluations, GMDS/ER assessments and the maternal interviews were stored in a lockable cupboard, so as to further assure participant confidentiality.

3.8 Statistical Analyses

Both descriptive and inferential statistics were employed in order to analyse variable data gathered during the collection procedure**.** Based on the conversion of the raw scores to *z* scores, as discussed in section 3.6.2, it was anticipated that distributions would be normal allowing for the use of stricter, more generalizable, parametric analyses. Graphical histograms of distribution outputs have been included (refer to Appendices D-I). While deviations from normal were slight, the presence of outliers was detected when using measures of central tendency, skewness, kurtosis coefficients and Kolmogorov-Smirnov test for normality, contributing to deviations in normality. As outliers were legitimate, with the potential to provide important information regarding development between groups, they were retained. While parametric tests are considered more robust and generally yield more statistical power, they are less sensitive to the presence of outliers. Hence, due to violations of normality and the inclusion of outliers, nonparametric analyses were deemed more appropriate, ensuring results would be interpreted with a degree of conviction.

Analyses were conducted using the Statistical Package for the Social Sciences (SPSS-19) (SPSS Inc, Chicago, IL). Frequency distributions and χ^2 tests was used for analysing categorical data. Descriptive data are shown as means, medians, SD and *Z* scores or number of observations (percentage). Continuous data between groups was analysed using the Kruskal–Wallis analysis of variance. Where significant results for interactions were obtained, further post-hoc analyses using Mann–Whitney U tests, were carried out controlling for the Type I error by using the Bonferroni correction, where the critical value of 0.5 is divided by the number of tests conducted (Field, 2009).

Differences over time points, *within* groups, was conducted using the Wilcoxan signed-rank test, while a series of Spearman's correlation coefficients (r_s) were calculated to determine the strength and direction of the relationship between subscales and the General Quotient (GQ) for each GMDS/ER version as well as between versions (Howell, 2002). Finally, correlations, using a series of Spearman's correlation coefficients (r_s) were used to determine the relationship between infant, maternal, pregnancy and lifestyle characteristics, known to be associated with adverse developmental outcomes at both Time 1 and Time 2, for each group. Further linear regressions were unable to be computed with certainty, due to missing data within the maternal data set.

All statistical analyses, were two tailed and unless otherwise noted were conducted at the (p<.05) level. However, due to the smaller sample size and to avoid erroneously rejecting the null hypothesis (Type I error) levels were deemed statistically significant at p< .001 (Howell, 2002). Precise p-values, as well as calculated effect sizes were reported for future meta-analyses to enhance research beyond statistical significance (Rosnow & Rosenthal, 1996).While statistical significance determines how likely an observed finding occurred by chance, the effect size measures the strength of the relationship between two variables and remains unaffected by sample size. The commonly used, Cohen's categories where, 0.2=small effect size; 0.5=medium effect size and 0.8=large effect size, were used for the interpretation of effect sizes (Cohen, 1988).

In summary, the methodology detailed in this chapter, systematically describes the exploratory and descriptive research method with special focus on, the sampling procedure of the sample, assessment measures used and statistical analyses conducted, in response to the three research

questions posed by the research study as derived from the main aims. The following chapter presents a detailed account of the results obtained.

Chapter 4 – Results

The purpose of this chapter is to present a statistical review of findings as collected from the data analyses conducted. The following section presents the descriptive analyses of the sample sets. Thereafter, guided by the study's research questions, inferential statistics are provided to address study aims, described in Chapter 3.

4.1 Descriptive Statistics

Based on the primary research aim to describe and compare the longitudinal developmental profiles of three groups of children with varying degrees of prenatal alcohol exposure, the following provides a summary of the sample datasets, enabling later inferences across groups, as well as between datasets and variables. As described in Chapter 3, participants were allocated to one of three groups based on their clinical diagnosis at 5years of age and level of prenatal alcohol exposure. Frequency Table 5 and Table 6 present the characteristics of infants and mothers, respectively within each group allocation.

Table 5 presents' descriptive baseline infant data where approximately a quarter of the sample had FAS/PFAS (24%, 29/121) based on the diagnostic criteria of either FAS or PFAS as described in Chapter 2 (Hoyme et al., 2005). Forty six per cent (56/121) were presented with some prenatal alcohol exposure forming the PAE group, while 30% (36/121) were assigned to the Control group. More than half the sample in each group were female (p=.056) with 80% of mixed ethnicity, and the remainder classified as black.

Table 5

Infant Characteristics based on Group Allocation (N=121)

Variable group	Category, n/N (%)	Control (36/121)	PAE (56/121)	FAS/PFAS (29/121)	*p*
Gender	Male	13/36 (36)	26/56 (46)	11/29 (38)	.056*
	Female	23/36 (64)	30/56 (54)	18/29 (62)	
Ethnicity	Black	7/36 (19)	10/56 (18)	7/29 (24)	<.001**
	Mixed Ethnicity	29/36 (81)	46/56 (82)	22/29 (76)	
	Birth weight mean z scores for age (IQR), n	0.40 (-0.03 to-0.14), 34[a]	0.45 (-0.41 to 0.67), 54[b]	-0.74 (-1.49 to -1.43), 25[a,b]	<.001**
	Less than 2.5kg	6/36 (17)	13/56 (23)	16/29 (55)	
New born Anthropometry †	Birth length mean z scores for age, (IQR), n	0.29 (-0.14 to 0.73), 32[a]	0.75 (-0.47 to 0.73), 53[b]	-0.36 (-0.80 to -0.07), 23[a,b]	.007*
	Birth OFC [Δ]mean z scores for age, (IQR), n	0.48 (-0.12 to 0.88), 33[a]	0.08 (-0.72 to 0.88), 53[b]	-0.32 (-0.14 to 0.07), 25[a,b]	.001**

Note. PAE=Prenatal Alcohol Exposure, FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome, IQR=inter-quartile range, †missing data, [Δ] refers to Occipital Head Circumference; Chi-square for discrete variables; Kruskal-Wallis for continuous variables; Variables sharing a subscript are significantly different from each other according to Mann-Whitney post hoc tests, using the Bonferroni correction where p=0.017, * p<0.05; ** p<0.001

Using the Chi-square and Kruskal-Wallis statistical tests for discrete and continuous variables, respectively, it is apparent from Table 5 that significant differences exist between groups over all infant characteristics. New born anthropometric measurements describe those with FAS/PFAS as being significantly smaller than the PAE and Control groups for weight (p<.001), length (p=.007) and head circumference (p<.001). Regardless of their clinical diagnosis, 29% of all infants were underweight, ≤ 2.5 kg at birth (35/121), with the majority being from the FAS/PFAS group (55%, 16/29).

Based on group allocation, Table 6 provides details of the maternal characteristics of the study sample.

Table 6

Maternal Characteristics based on Group Allocation (N=121)

Variable group	Category, n/N (%)	Control (36/121)	PAE (56/121)	FAS/PFAS (29/121)	*p*
Age†	Mean yrs (sd), n	25.7 (6.43), 34[a]	26.43 (6.18), 55[b]	31.14 (6.64), 28[a,b]	.002*
Marital Status†	Married/Engaged	9/32 (25)	14/54 (25)	5/29 (17)	<.001**
	Divorced/ Widowed	1/32 (3)	3/54 (6)	-	
	Unmarried, living with partner	5/32 (14)	14/54 (30)	16/29 (55)	
	Single	17/32 (47)	23/54 (43)	8/29 (28)	
Level of Education †	No formal schooling	1/32 (3)	2/53 (4)	6/28 (21)	<.001**
	Incomplete Primary School	3/32 (9)	8/53 (15)	9/28 (32)	
	Complete Primary School	3/32 (9)	10/53 (18)	4/28 (14)	
	Incomplete Secondary School	11/32 (34)	25/53 (47)	9/28 (32)	
	Complete Secondary School	14/32 (44)	8/53 (14)	-	
Maternal Occupation †	Full time	10/32 (28)	10/53 (18)	1/29 (3)	<.001**
	Part time	6/32 (19)	10/53 (18)	5/29 (17)	
	Unemployed	16/32 (50)	33/53 (62)	23/29 (79)	

Note. PAE=Prenatal Alcohol Exposure, FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome, IQR= inter-quartile range, †missing data, Hx=history, Chi-square for discrete variables; Kruskal-Wallis for continuous variables; Variables sharing a subscript are significantly different from each other according to Mann-Whitney posthoc tests, using the Bonferroni correction, where p=0. 017,* p<0.05; **p<0.001

There is a significant difference (p<.05) between groups over all maternal characteristics, with mothers of children with FAS/PFAS, 5-6 years older (mean=31.14 years; p=.002) and unmarried but cohabiting with their partners (55%, 16/26; p<.001). Most mothers (69%) in the study group were unmarried. Particularly low levels of maternal education emerged amongst mothers of FAS/PFAS children, with 32% having incomplete primary schooling. Mothers in the Control group were more likely to have completed high school (44%; 14/32) and be in full time employment (28%, 10/32 versus 3% of FAS/PFAS, 1/29). A large number of mothers across all

three groups were unemployed (63%; 72/114). Descriptive information, based on group allocation, related to pregnancy and lifestyle variables are presented in Table 7.

Table 7

Pregnancy and Lifestyle Variables based on Group Allocation (N=121)

Variable group	Category, n/N (%)	Control	PAE	FAS/PFAS	*p*
Parity	Mean # of children (sd), n	1.91 (1.97), 35[c]	2.41 (1.41), 56	2.79 (1.18), 29[c]	.027*
	Death of a Child	4/35 (11)	9/56 (16)	11/29 (40)	
Month pregnancy discovered†	Mean, months (sd), n	3.06 (1.47), 25	3.82 (1.35), 33	4.22 (1.91),9	.067
Length Breastfed†	None	4/32 (11)	3/56 (5)	3/29 (10)	
	Mean, months (sd), n	13.93 (12.09), 28	18.04 (11.84), 51	14.81 (10.10), 26	.267
Smoking†	Currently smoking	7/35 (19)	18/55 (32)	4/28 (14)	
	Within last year	1/35 (3)[a,b]	13/55 (24)[b,c]	18/28 (64)[a,c]	<.001**
	More than a year ago	-	16/35 (11)	2/28 (7)	
	Never smoked	27/35 (75)	18/55 (32)	4/28 (14)	
Smoking in pregnancy†	n/N (%)	7/36 (19)[a,b]	29/55 (53)[c]	22/29 (76)[a]	<.001**
Alcohol use prior to pregnancy†	Units per week, median, (range) n	.00 (4), 36[a,b]	13 (141), 47[b,c]	31 (210), 24[a,c]	<.001**
Alcohol use in pregnancy†	Units per week, median, (range) n	0 (0), 36[a,b]	7 (141), 48[b,c]	46 (217), 25[a,c]	<.001**

Note. PAE=Prenatal Alcohol Exposure, FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome, IQR= inter-quartile range, †missing data, Hx=history, Chi-square for discrete variables; Kruskal-Wallis for continuous variables; Variables sharing a subscript are significantly different from each other according to Mann-Whitney posthoc tests, using the Bonferroni correction where p=0.017, * p<0.05; **p<0.001

While a few years older than other groups, mothers of infants with FAS/PFAS had substantially more children than expected (p=.027). About 40% (11/29) of mothers from the FAS/PFAS group had experienced the death of a child in the family compared to 11% (4/35) in the Control Group. Most mothers discovered their pregnancy with the child of interest between 4-6 months (p=.067). Only a minority of participants (9%) indicated never having breastfed the child of interest (COI), with most having breastfed for 12 to 24 months.

Almost two thirds of mothers of FAS/PFAS infants smoked within the last year and a high proportion smoked during pregnancy, more than the PAE and Control groups. As expected, maternal alcohol consumption both prior to and during pregnancy was substantially higher amongst mothers in the FAS/PFAS group, with mean alcohol units per week increasing from 46 prior pregnancy to 61.8 during pregnancy (p<.001). Mothers in the FAS/PFAS group reported drinking very heavy levels of alcohol (10/24; 42%) prior to the confirmation of pregnancy, compared to reported moderate levels (8–25 units) by those in the PAE group 28% (13/47) (p<.001; z = -7.884). During pregnancy, 60% of mothers from the FAS/PFAS group reported drinking very high levels of alcohol (≥36 units per week), with 23% from the PAE group drinking low levels, less than 7 units per week of alcohol (p<.001; z= -6.228).

Prior to presenting the developmental differences between groups, the following provides a description of the performance, per group, over each subscale of the GMDS/ER. While customary to use medians rather than means when dealing with non-normal distributions, both are included as they are not appreciably different from one another.

The following tables provide a summary of the raw means, medians and standard deviations for all GMDS/ER subscales and the General Quotient (GQ) at Time 1 (see Table 8 and Time 2 (see Table 9).

Table 8

Descriptive Statistics for groups over the GMDS subscales at Time 1

	Control (36/121)					PAE (56/121)					FAS/PFAS (29/121)				
GMDS Subscales	Min	Max	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max	Mean	Median	SD
Locomotor	22	44	28.9	28.0	4.77	13	38	28.29	29.0	4.69	12	35	25.45	26.0	4.84
Personal-Social	29	44	33.5	33.0	3.15	24	42	33.09	32.0	3.61	18	39	31.24	32.0	4.11
Hearing-Language†	24	42	28.9	28.0	3.61	23	37	28.55	28.0	3.26	18	33	26.86	26.0	3.17
Eye-Hand Coordination	25	45	28.4	27.0	3.92	23	37	27.82	27.0	3.17	11	33	25.86	26.0	4.50
Performance	23	51	27.2	26.0	5.02	19	36	26.25	26.0	3.49	15	34	24.93	25.0	3.95
GQ General Quotient	25	45	29.3	28.0	3.70	21	35	28.77	28.0	2.96	17	33	26.66	27.0	3.54

Note. Time 1=7-12 months of age; GMDS=Griffiths Mental Developmental Scales; PAE=Prenatal Alcohol Exposure; FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome, † referred to Hearing-Language in the infant version of the GMDS, but as Language in the older version.

As shown in Table 8, on average, infants aged 7-12 months of age with FAS/PFAS performed lower overall subscales as measured by the GMDS, when compared to the other two groups. The developmental profile of infants with some prenatal alcohol exposure (PAE group) tends to follow a similar pattern to that of the Control group, rather than the FAS/PFAS group. In other words the PAE group performed better than expected and favourably compared to the overall performance of those with no prenatal alcohol exposure.

Table 9

Descriptive Statistics for groups over the GMDS/ER subscales at Time 2

	Control (36/121)					PAE (56/121)					FAS/PFAS (29/121(				
GMDS Subscales	Min	Max	Mean	Median	SD	Min	Max	Mean	Median	SD	Min	Max	Mean	Median	SD
Locomotor	20	82	70.22	71.0	10.82	20	92	69.89	70.0	12.17	40	92	61.0	62.0	13.37
Personal-Social	32	88	76.17	77.0	10.22	32	90	72.23	74.0	11.21	56	98	63.59	64.0	12.63
Language	21	66	50.33	48.0	10.67	21	68	46.13	46.0	9.37	34	78	44.31	40.00	12.27
Eye-Hand Coordination	27	76	57.94	55.0	14.46	27	86	51.39	50.0	11.56	36	90	43.03	39.0	11.14
Performance	25	64	52.17	48.0	14.09	26	58	43.82	44.0	7.44	34	94	39.72	38.0	10.35
Practical Reasoning	24	72	59.56	61.0	13.54	24	80	51.57	52.0	11.44	38	88	45.86	46.0	12.14
GQ General Quotient	25	74	61.06	60.0	10.22	25	70	55.84	57.0	7.54	45	88	49.55	48.0	10.28

Note. Time 2=5 years of age; GMDS/ER=Revised- Griffiths Mental Developmental Scales; PAE=Prenatal Alcohol Exposure; FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome; † referred to Hearing-Language in the infant version of the GMDS, but as Language in the older version.

At 5 years of age, the FAS/PFAS group continues to perform poorly, with stark differences emerging between groups over all subscales, as demonstrated in Table 9. While during infancy, the developmental pattern of the PAE group followed that of the Control Group, with age, gaps between the PAE and Control group widen, with performance of the PAE group now typically following that of the FAS/PFAS group.

In summary, children with FAS/PFAS performed significantly worse than those with some or no prenatal alcohol exposure at both Times 1 and 2. During infancy, while those with some prenatal alcohol exposure during infancy performed within age appropriate limits, results of a Kruskal–Wallis test described in section 4.2.1 reveal statistically significant differences emerging with

age, with developmental profiles for this group emulating that of the FAS/PFAS group rather than the Control group, as observed at Time 1 assessment.

The following section presents the inferential statistics conducted during the data analyses procedure.

4.2 Inferential Statistics

For parametric statistical analyses normality of the data is a prerequisite. While many distributions were normal in the current data set, there was concern regarding the presence of outliers known to contribute to the deviation in the distribution of variables, discussed in Chapter 3. Ultimately, it was decided that non-parametric analyses would be more appropriate, with findings being interpreted with more conviction. Guided by each research question, the following section presents these inferential findings to determine the nature and statistical significance of relationships between groups, time points and variables.

4.2.1 Research question 1.

What developmental differences exist between the three groups (Control, PAE and FAS/PFAS) over a period of 5 years?

Research Question 1 sought to describe the differences *between* groups at two time points, as well as differences *within* groups over time. A series of Kruskal-Wallis tests were conducted to evaluate differences on median change at Time 1 (see Table 10) and at Time 2 (see Table 11) between the three groups (Control, PAE, and FAS/PFAS).

Table 10

Kruskal–Wallis Summary Table of Differences between Groups at 7-12 months of age, Time 1

	Control (n=36)	**PAE (n=56)**	**FAS/PFAS (n=29)**		
GMDS Subscale	Mean Rank	Mean Rank	Mean Rank	*H(2)*	*p*
Locomotor (AQ)	66.04[a]	65.63[b]	45.79[a,b]	7.22	.027*
Personal-Social (BQ)	67.44	63.10	48.95	4.90	.087
Hearing-Language†(CQ)	68.74[a]	66.86[b]	40.09[a,b]	13.76	.001**
Eye-Hand Coordination (DQ)	67.56	62.53	49.91	4.34	.114
Performance (EQ)	66.32	62.62	51.28	3.22	.200
General Quotient (GQ)	68.79a	65.07b	43.47[a,b]	9.98	.007*

Note. GMDS=Griffiths Mental Developmental Scales; PAE = Prenatal Alcohol Exposure; FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome,† = referred to as Language scale used in GMDS/ER; Based on the Bonferroni correction, mean ranks sharing a subscript are significantly different, at the p <.017 from each other , * $p<0.05$; ** $p<0.001$

At Time 1, significant developmental differences emerged between groups over the Locomotor (H (2) =7.22, p=.027) and Hearing-Language (H (2) =13.76, p=.001) subscales, as well as the General Quotient (H(2)=9.98, p=.007). Post hoc comparisons, using a series of Mann-Whitney U tests were performed to follow up statistical findings. The Bonferroni correction was used to correct for Type I error rate during the multiple comparison procedure. Post hoc comparison effects are reported at the p=.017 level of significance.

Infants with FAS/PFAS performed significantly poorer than their counterparts from both the PAE and Control groups, over gross motor (FAS/PFAS vs. PAE, z= -2.39, r= -.26, p=.016; FAS/PFAS vs. Control, z= -2.44, r= -.30, p=.015), receptive and expressive language (FAS/PFAS vs. PAE, z= -3.30, r= -.36, p=.001; FAS/PFAS vs. Control, z= -3.35, r= -.42,

p=.001) and overall developmental ability (FAS/PFAS vs. PAE, *z*= -2.69, *r*= -.29, *p*=.008; FAS/PFAS vs. Control, *z*= -2.94, *r*= -.04, *p*=.003).

During infancy, small differences in effect size over specific developmental subscales, between the FAS/PFAS and PAE groups suggest similar levels of developmental functioning with similar effect size differences observed between the FAS/PFAS and Control groups. A larger difference in effect size was reported over the Hearing-Language scale (*r*=.42), suggesting developmental achievement over language abilities during infancy, may be related to the level of maternal alcohol exposure.

With age, differences between the three study groups became more apparent, presented in Table 11. At Time 2, using the Kruskal–Wallis test, small developmental differences emerged over all but the Language subscale (*H* (2) =5.19, *p*=.075). Further, Mann–Whitney post hoc comparisons, using the Bonferroni correction, revealed that the FAS/PFAS group performed significantly worse than the PAE group over the Locomotor (*z*= -3.03, *r*= -.33, *p*=.003), Personal-Social (*z*= -3.12, *r*= -.34, *p*=.002), and Eye–Hand Coordination (*z*= 03.57, *r*= -.39, *p*<.001) subscales, as well as on the General Quotient (*z*=-3.48, *r*= -.38, *p*=.001).

Table 11

Kruskal–Wallis Summary Table of Differences between Groups at 5 years of age, Time 2

	Control	**PAE**	**FAS/PFAS**		
	(n=36)	**(n=56)**	**(n=29)**		
GMDS Subscale	Mean Rank	Mean Rank	Mean Rank	*H(2)*	*p*
Locomotor (AQ)	68.00[a]	66.35[b]	41.98[a,b]	11.31	.003*
Personal-Social (BQ)	73.61[a]	64.11[b]	39.34[a,b]	16.20	.000**
Language†(CQ)	71.15[a]	59.26	51.76[a]	5.19	.075
Eye-Hand Coordination (DQ)	77.99[a]	62.79[b]	36.47[a,b]	22.84	.000**
Performance (EQ)	78.78[a,c]	59.13[c]	42.55[a]	17.56	.000**
Practical Reasoning (FQ)	77.47[a,c]	59.83[a,c]	42.81[a]	15.85	.000**
General Quotient (GQ)	77.21[a]	62.96[b]	37.09[a,b]	21.38	.000**

Note. GMDS=Griffiths Mental Developmental Scales; PAE =Prenatal Alcohol Exposure; FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome,†= referred to as Hearing–Language in GMDS scale; Based on the Bonferroni correction, mean ranks sharing a subscript are significantly different, at p <.0167, from each other
* $p < 0.05$; ** $p < 0.001$

At 5 years of age, negligible differences in effect sizes between groups with prenatal alcohol exposure (FAS/PFAS and PAE) propose similar patterns of developmental functioning. While a small difference in effect size (r=0.3) was reported over the Language subscale, all other subscales show medium effect size differences, suggesting recognizable variations in developmental functioning between these two groups over specific developmental domains at 5 years of age. The FAS/PFAS group continued to perform poorly, when compared to the Control group, revealing significant differences over all subscales and the General Quotient (z= -4.21, r=.-.50, p<.001).

While no significant differences between the PAE and Control groups were reported at Time 1 (during infancy), results at 5 years of age suggest that the children with some prenatal alcohol exposure performed significantly worse on abilities associated with visual-spatial reasoning (z= -2.78, r=-.29, p=.006) and concept formation (z= -2.51, r=-.26, p=.011) when compared to those with no alcohol exposure. Small differences in effect size between the PAE and Control groups suggest both groups display similar levels developmental profiles. Differences in the GQ at both Time 1 and Time 2 are likely due to differences over subscales within the GMDS/ER, which contribute to overall developmental ability. Furthermore, significant levels described may reflect differences in the sample size between groups.

In summary, findings suggest that alcohol exposure during pregnancy contributes to developmental delays between groups; with those more heavily exposed presenting with poorer overall developmental profiles, both as infants and continued into early childhood. With age, considerably more significant differences were found between groups over the subscales of the GMDS/ER, with less chance of catch up with significant negative effects apparent, even at lower levels of exposure at 5 years of age.

To determine differences between time points, *within* groups, a series of Wilcoxon Signed Rank tests were conducted over all but the Practical Reasoning subscales of the GMDS/ER. This higher-order cognitive subscale was removed from the analyses, as it only forms part of the older GMDS/ER scale set assessed at Time 2, therefore no baseline Time 1 data was available for comparison.

Table 12

Group Differences between Time 1 and Time 2 Assessments

				95%CI			
GMDS/ER Subscale	Study Group	*N*	*Z*	LL	UL	*p*	*r*
	Control	36	-.64	.510	.536	.523	-.08
Locomotor	PAE	56	-.97	.327	.351	.339	-.09
	FAS/PFAS	29	-.01	.993	.997	.995	-.00
	Control	36	-1.30	.190	.211	.201	-.15
Personal–Social	PAE	56	-.58	.551	.576	.563	-.05
	FAS/PFAS	29	-.72	466	.492	.479	-.01
	Control	36	-.82	.410	.435	.422	-.10
Language†	PAE	56	-1.13	.244	.266	.255	-.11
	FAS/PFAS	29	-1.40	.160	.180	.170	-.18
	Control	36	-1.87	.052	.084	.059	-.22
Eye-Hand Coordination	PAE	56	-.47	.625	.650	.638	-.04
	FAS/PFAS	29	-.96	.343	.368	.356	-.13
	Control	36	-2.11	.029	.038	.034*	-.25
Performance	PAE	56	-.14	.883	.899	.891	-.01
	FAS/PFAS	29	-.77	.438	.464	.451	-.10
	Control	36	-1.89	.053	.085	.059	-.22
General Quotient	PAE	56	-.38	.703	.726	.715	.04
	FAS/PFAS	29	-.39	.890	.714	.702	-.05

Note. Time 1=7-12 months; Time 2=5 years of age; GMDS/ER=Griffiths Mental Developmental Scales/ Revised; PAE =Prenatal Alcohol Exposure; FAS=Fetal Alcohol Syndrome, PFAS=Partial Fetal Alcohol Syndrome, †=referred to as Hearing –Language in Time 1scale; * $p < 0.05$

As presented in Table 12, findings for both the FAS/PFAS and PAE groups reveal no significant differences between assessments at Time 1 and Time 2, while for the Control group, significant differences emerged over only the Performance scale (z= -2.11,r =-.25 , p=.034). Using the

converted *z* score median values, Figure 4 offers an alternative representation of findings for both the FAS/PFAS and Control groups performance's at Time 1 and 2.

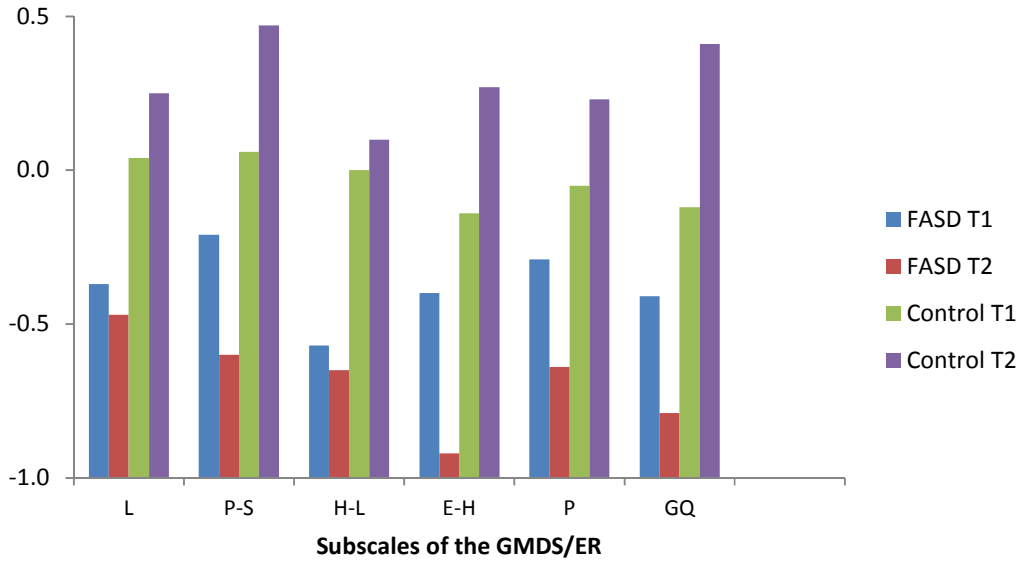


Figure 4. Developmental achievement between the FAS/PFAS (n = 24) and Control (n = 36) groups over Time 1 and Time 2

As illustrated above, the performance of the FAS/PFAS group over all developmental subscales at Time 1 remains well below the mean (*m*=0), with a delay of more than half of the mean evident on the Hearing-Language subscale (ZT_1= -.57). While the Control group appeared to perform better than the FAS/PFAS group at Time 1, the former children with no prenatal alcohol exposure performed below the mean on the higher–order construct subscales of Eye-Hand Coordination(ZT_1= -.14) and the Performance (ZT_1= -.05) subscales. With age, the FAS/PFAS group continued to show delays with marked declines in achievement on Personal–Social (ZT_2= -.60); Eye–Hand coordination (ZT_2= -.92) and Performance (ZT_2= -.64) subscales, as well as the General Quotient (ZT_2= -.79). In contrast, at 5 years of age, the Control group indicates

improved performance over all subscales when compared to their infant assessment, with significant differences emerging on the Performance subscale (z= -2.11,r =-.25 ,p =.034).

Figure 5 illustrates the developmental profile of the PAE group compared to those with no prenatal alcohol exposure of the Control group.

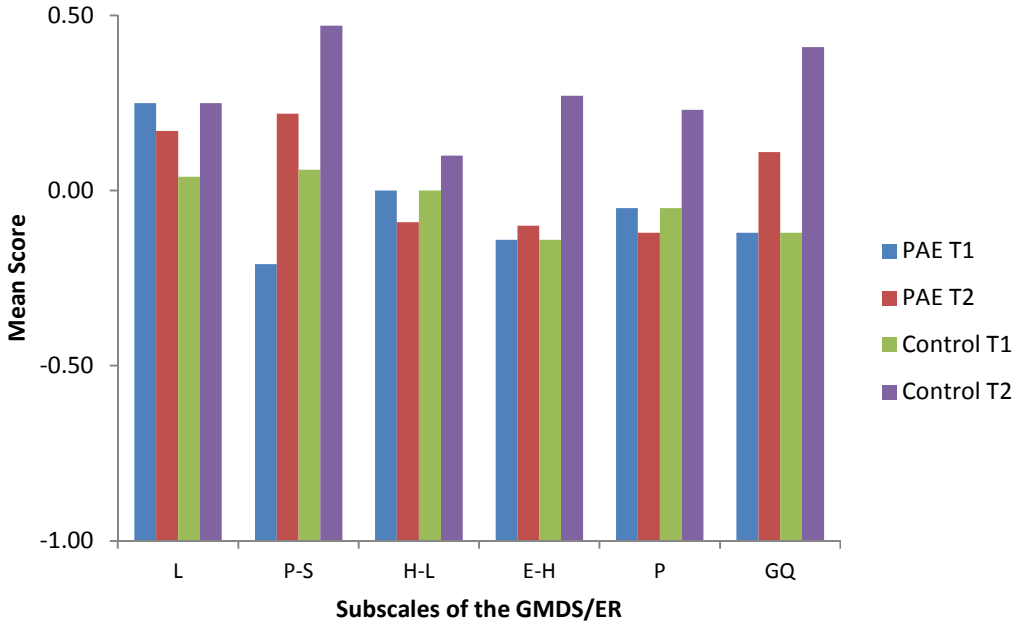


Figure 5. Developmental achievement of the PAE (n=56) and Control groups (n=36) over Time 1 and Time 2

The developmental profile of the PAE group mirrors that of the Control group during infancy. Findings reveal that developmental scores of infants with some prenatal alcohol exposure fall below the mean over all but the gross motor (ZT_1=.25) and Hearing–Language (ZT_1=0) subscales. However, by 5 years of age the performance of the PAE group tends to follow that of

the FAS/PFAS rather than the Control group. Gross motor (ZT_2=.17), language (ZT_2=-.09) and visual-spatial reasoning (ZT_2=-.12) abilities within the PAE group, decrease when compared to their Time 1 performance, while increases emerged over the Personal–Social (ZT_2=.22) and Eye–Hand Co-ordination subscales (ZT_2=-.10), as well as the General Quotient (ZT_2=.11).

Similar small differences in effect sizes to those reported for the FAS/PFAS group, suggest comparable developmental functioning between assessments for the PAE, while medium differences in effect size observed within the Control group over the Performance subscale (ZT_2=.23), suggests practical differences between Time 1 and Time 2 scores.

These findings suggest that while infants with heavy prenatal alcohol exposure perform worse when compared to those with some or no prenatal alcohol exposure, over most developmental domains, with age little improvement is identified. Infants with some prenatal alcohol exposure (PAE group) tend to perform better than their FAS/PFAS group counterparts during infancy, but by 5 years of age developmental profiles compare to the FAS/PFAS group's performance. Finally, while the Control group performed better than both the FAS/PFAS and PAE groups over most developmental subscales at Time 1 and Time 2, developmental performance within this non-exposed group from this community revealed average to below average scores as reported by the GMDS/ER. Reasons for observed group fluctuations in performance are discussed in Chapter 5.

4.2.2 Research question 2.

What is the relationship between infant developmental performance over subscales, measured by the Infant version of the GMDS (Time 1) and achievement at 5 years of age (Time 2) measured by the Child Version GMDS/ER?

The following section describes the findings conducted for Research Question 2 of the association *between* versions of the GMDS/ER, for each group, over time. Since some variables were not normally distributed, the nonparametric Spearman's correlation coefficient was calculated to determine the relationship between subscales and general quotient (GQ) performance *between* versions of the GMDS and GMDS-ER, respectively (as highlighted in Table 13).

Regardless of prenatal alcohol exposure, findings indicate no significant correlations between subscales as assessed by the Infant version of the GMDS and later performance at 5 years of age, using the GMDS/ER. This outcome may be due to the small sample size and the presence of outliers, known to impact correlational analyses. In an attempt to increase the sample size, groups were collapsed, with findings indicating significant relationships between infant gross motor abilities, assessed during infancy by the Locomotor subscale of the GMDS and visual-spatial reasoning at 5 years of age on the Performance subscale (r_s=.20, p=.025) of the GMDS/ER. In other words, infants with higher language scores showed better scores at 5 years of age over the Personal–Social subscale *(*r_s=.22, p=.014). Essentially, these findings suggest that the developmental constructs being assessed by the GMDS/ER during infancy and early childhood are poorly correlated. Furthermore, they may describe the overlap in abilities between subscales over different versions of the GMDS/ER.

Table 13

Intercorrelations between subscales of the GMDS and GMDS-ER over time

GMDS/ER Subscales	Study Group	GMDS-ER Subscales						
		Time 2						
Time 1	(n/N)	1	2	3	4	5	6†	7
1. Locomotor	Full (121)	.01	.16	.01	.13	.20*	.06	.11
	Control (36)	-.19	.05	-.06	-.04	.08	-.01	-.06
	PAE (56)	-.04	.09	-.03	.09	.07	.12	.06
	FAS/PFAS (29)	-.07	.09	-.09	.15	.28	-.08	.02
2. Personal-Social	Full (121)	-.02	.17	.01	.09	.03	.03	.06
	Control (36)	-.28	.03	-.25	.00	-.20	-.05	-.11
	PAE (56)	-.08	.09	.01	-.08	-.07	-.05	-.05
	FAS/PFAS (29)	.19	.19	.14	.20	.20	.01	.15
3. Language	Full (121)	.12	.22*	.03	.16	.14	.16	.16
	Control (36)	-.04	.02	.02	.09	.29	.25	.15
	PAE (56)	-.05	.09	-.18	-.03	-.18	-.03	-.11
	FAS/PFAS (29)	.23	.20	.18	.16	.13	.04	.18
4. Eye-Hand Coordination	Full (121)	-.04	.16	-.05	.11	.02	.05	.05
	Control (36)	.00	.20	.14	.23	.11	.23	.20
	PAE (56)	.-.26	.04	-.23	-.06	-.24	-.12	-.19
	FAS/PFAS (29)	.17	.13	.05	.07	.10	-.05	.04
5. Performance	Full (121)	.09	.05	.07	.15	.17	.04	.12
	Control (36)	-.08	.02	.01	.14	.13	.17	.09
	PAE (56)	.01	-.11	-.04	.07	.08	-.11	-.00
	FAS/PFAS (29)	.24	.16	.23	.10	.20	.03	.17
6. Practical Reasoning†	Full (121)	.06	.03	.16	.05	.04	†	.11
	Control (36)	-.01	-.05	.25	.23	.17	†	.14
	PAE (56)	.02	-.05	-.03	-.12	-.11	†	.00
	FAS/PFAS (29)	-.08	.01	.04	-.05	.03	†	.02
7 General Quotient (GQ)	Full (121)	.07	.24*	.04	.21*	.18*	.11	.17
	Control (36)	-.11	.15	.00	.11	.12	.14	.09
	PAE (56)	-.05	.14	-.05	.11	.04	.00	.05
	FAS/PFAS (29)	.25	.22	.12	.22	.22	02	.16

Note. Time 1–7-12 months; Time 2 =5 years of age, Δ referred to as Speech–Hearing subscale at Time 1 and Language at Time 2*;* †subscale 6=Practical Reasoning subscale only included in older child version,* **p* <0 .01; **p* <0.05

The following section provides a description of the analyses conducted for Research Question 3 which seeks to identify the relationships between infant, maternal and pregnancy and lifestyle variables on developmental performance over two time points during early childhood.

4.2.3 Research question 3.

Which socio-demographic variables are most strongly related to childhood development for each of the three groups?

In considering normality, the Spearman's Correlation Coefficient (r_s) was utilized to assess the relationship between early childhood developmental achievements and socio-demographic variables. The following section presents the correlational results for each group, based on infant demographics (see Table 14), maternal variables (see Table 15) and maternal lifestyle and pregnancy variables, described in Table 16.

Table 14 presents the correlation coefficients (r_s) for each group at Time 1, based on infant variables, namely; birth weight, length and head circumference (OFC), as well as gender and ethnicity.

While no significant correlations between infant variables and developmental performance were reported for groups with prenatal alcohol exposure (FAS/PFAS, PAE), a negative correlation between gender and achievement on the fine motor subscale of the GMDS was observed for the Control group with boys typically performing poorer than girls during infancy (r_{pb}= -.35, p=.035).

Table 14

Correlations between infant variables and developmental performance over GMDS subscales at Time 1

GMDS Subscales	Study Group	Birth Weight	Birth Length	Birth OFC	Gender	Ethnicity
	Control	-.14†	-.30†	-.27†	-.12	.04
Locomotor	PAE	.17†	.18†	.02†	.05	.01
	FAS/PFAS	.31†	.07†	.22†	-.07	-.12
	Control	.02†	.12†	-.22†	-.29	.04
Personal-Social	PAE	.09†	-.03†	-.09†	.13	.01
	FAS/PFAS	.06†	.18†	.33†	.05	.02
	Control	.08†	-.04†	-.06†	-.28	.09
Speech-Hearing	PAE	.06†	-.07†	.01†	.09	.02
	FAS/PFAS	-.03†	.02†	.05†	-.05	-.09
	Control	.29†	.04†	-.18†	-.35*	-.18
Eye-Hand Coordination	PAE	-.07†	-.11†	-.10†	.16	.00
	FAS/PFAS	.17†	.26†	.21†	.10	.15
	Control	.04†	.12†	-.30†	-.19	-.05
Performance	PAE	.05†	-.07†	.06†	.21	.09
	FAS/PFAS	.13†	.34†	.14†	.10	.19
	Control	-.04†	-.04†	-.30†	-.30	.03
General Quotient (GQ)	PAE	.17†	.07†	.07†	.16	.02
	FAS/PFAS	.22†	.14†	.20†	-.01	.08

Note. Time 1=7-12 months of age, OFC=occipital frontal circumference, †=missing data, *$p < 0.05$

Table 15 presents the correlations between maternal variables and developmental performance over the subscales of the GMDS assessed during infancy.

Table 15

Correlations between maternal variables and developmental performance over GMDS subscales at Time 1

GMDS Subscales	Study Group	Maternal Age	Marital Status	Mothers Grade	Employment	Children Alive
	Control	-.10†	-.08†	.28†	-.07†	-.09†
Locomotor	PAE	.06†	-.09†	.04†	-.12†	-.02
	FAS/PFAS	.08†	-.30	-.10†	-.27	-.07
	Control	-.24†	.21†	.26†	-.05†	-.32†
Personal-Social	PAE	.08†	.12†	.02†	-.37†**	-.08
	FAS/PFAS	.28†	.02	-.20†	-.14	.16
	Control	-.17†	.05†	.14†	-.15†	-.49†**
Speech-Hearing	PAE	.14†	-.01†	-.24†	-.38†**	.01
	FAS/PFAS	.03†	.03	-.05†	-.05	-.29
	Control	-.08†	-.05†	.42†*	-.27†	-.08†
Eye-Hand Coordination	PAE	.11†	.05†	-.33†**	-.26†	-.01
	FAS/PFAS	.08†	.16	-.23†	-.28	-.01
	Control	-.24†	.11†	.30†	-.26†	-.40†*
Performance	PAE	-.11†	.12†	-.04†	-.15†	-.12
	FAS/PFAS	.13†	.23	-.06†	-.11	-.11
	Control	-.25†	.03†	.34†	-.18†	-.39†*
General Quotient (GQ)	PAE	.02†	.03†	-.08†	-.24†	-.09
	FAS/PFAS	.15†	.11	-.15†	-.17	-.08

Note. Time 1=7-12 months of age, †=missing data, *p <0 .05, ** p <0 .01

Results during infancy, within the PAE group, indicate lower levels of maternal education are associated with poorer fine motor performance (r_s= -.33, p=.016), while unemployment relates to decreased performance over Personal–Social (r_s=-.37, p=.006) and Language (r_s=-.38, p=.005)

abilities. Non-exposed infants with larger families are associated with poorer performance over Language (r_s=-.49, p=.003) and Performance (r_s=-.40, p=.018) subscales, as well as the General Quotient (r_s=-.39, p=.022). Decreased fine motor performance in the Control group, was linked with males (r_{pb}= -.35, p=.035) and a later recognition of pregnancy (rs= -.06, p=.002) while the level of maternal education (r_s=.42, p=.016) relates to better performance over fine motor outcomes. No significant correlations were reported within the FAS/PFAS group.

Table 16 presents the correlations between variables associated with maternal lifestyle during the child of interest's pregnancy. The later a mother confirmed her pregnancy, the worse infants with FAS/PFAS perform over the Personal–Social (r_s= -.71, p=.031) and Language (r_s= -.81, p=.008) subscales, which suggest the far reaching implications of prenatal alcohol exposure during early pregnancy. Similar findings were reported amongst the Control group with poor scores identified on fine motor (r_s= -.60, p=.002) abilities. No significant relationships emerged between maternal lifestyle and pregnancy variables and infants from the PAE group, at Time 1. Furthermore, during infancy, no significant associations between levels of alcohol consumption prior to and during pregnancy emerged over any of the groups.

Table 16

Correlations between maternal lifestyle and pregnancy variables and developmental performance over GMDS subscales at Time 1

GMDS Subscales	Study Group	Month preg	Length Breastfeeding	# of Cig prior preg	# of Cig during	Total units of alc prior	Total units of alc during
Locomotor	Control	-.35†	-.28†	.00†	.09†	.08	-
	PAE	-.11†	.07†	-.02†	.04†	-.17†	-.10†
	FAS/PFAS	-.29†	-.10†	.08†	.13†	.16†	.35†
Personal-Social	Control	-.29†	.23†	-.12†	-.17†	-.24	-
	PAE	-.04†	.15†	-.07†	-.06†	-.10†	-.10†
	FAS/PFAS	-.71†*	-.01†	-.14†	.02†	.01†	.15†
Language	Control	.22†	-.02†	-.11†	-.03†	-.13	-
	PAE	.07†	.04†	.09†	.02†	-.09†	-.20†
	FAS/PFAS	-.81†**	.16†	.01†	.13†	.00†	.07†
Eye-Hand Coordination	Control	-.60†**	-.00†	-.14†	-.04†	-.16	-
	PAE	-.10†	.05†	.15†	.10†	.02†	-.17†
	FAS/PFAS	-.26†	-.04†	-.07†	-.00†	.11†	.29†
Performance	Control	-.28†	-.06†	-.22†	-.27†	-.27	-
	PAE	-.06†	.02†	.13†	.18†	.08†	-.17†
	FAS/PFAS	-.54†	-.11†	-.07†	.06†	.14†	.19†
General Quotient (GQ)	Control	-.32†	-.04†	-.14†	-.11†	-.17	-
	PAE	-.07†	.07†	-.04†	-.03†	-.16†	-.21†
	FAS/PFAS	-.60†	.03†	-.04†	.10†	.03†	.21†

Note. Time 1=7-12 months of age, Preg=pregnancy; #=number, Cig =cigarettes, alc=alcohol, †=missing data, *p <0 .05, ** p <0 .01

The following section presents the findings of the associations between the same infant (see Table 17), maternal (see Table 18) and lifestyle and pregnancy (see Table 19) variables on developmental achievement at 5 years of age (Time 2) using the GMDS/ER.

Table 17

Correlations between baseline infant variables and developmental performance over GMDS/ER subscales at Time 2

GMDS/ER Subscales	Study Group	Birth Weight	Birth Length	Birth OFC	Gender	Ethnicity
	Control	-.09†	.26†	-.06†	.03	-.25
Locomotor	PAE	.32†*	.39†**	.41†**	-.06	-.16
	FAS/PFAS	.10†	.22†	.18†	-.20	.33
	Control	-.11†	.04†	-.15†	-.05	-.27
Personal- Social	PAE	.32†*	.31†*	.37†**	.20	-.02
	FAS/PFAS	-.02†	.23†	.12†	.01	.12
	Control	-.07†	.01†	-.37†*	-.08	-.51**
Language	PAE	.12†	.17†	.28†*	.10	.13
	FAS/PFAS	-.04†	.31†	-.14†	.15	.12
	Control	.12†	.22†	-.21†	.08	-.42*
Eye-Hand Coordination	PAE	.31†*	.38†**	.29†*	.17	.10
	FAS/PFAS	.12†	.12†	.16†	-.20	.09
	Control	-.05†	-.05†	-.19†	.03	.01
Performance	PAE	.31†*	.30†*	.29†*	.06	.05
	FAS/PFAS	.19†	.25†	.02†	-.03	.02
	Control	.04†	.13†	-.26†	-.11	-.38*
Practical Reasoning	PAE	.16†	.08†	.09†	.06	-.09
	FAS/PFAS	-.06†	.10†	-.18†	.06	.13
	Control	.08†	.17†	-.24†	-.05	-.40*
General Quotient (GQ)	PAE	.35†*	.38†**	.38†**	.13	-.02
	FAS/PFAS	-.02†	.19†	.05†	-.10	.10

Note. Time 1=7-12 months of age, OFC=occipital frontal circumference, †=missing data, *p <0 .05

Table 17 describes the association between baseline infant variables collected at Time 1 with developmental achievement over the GMDS/ER subscales at 5 years of age. Results obtained for the PAE group at Time 2 describe significant positive correlations between birth weight (BW) and birth length (BL) over all but the Language (BW, r_s=.12, p=.402, BL, r_s=.17, p=.232) and Practical Reasoning (BW, r_s=.16, p=.239, BL, r_s=.08, p=.589), with infants with larger birth anthropometric measurements performing better over the identified subscales. Furthermore, significant associations between head circumference at birth suggest better developmental outcomes at 5 years of age over all but the Practical Reasoning (r_s=.09, p=.543) subscale for children in the PAE group. Language proved the most heavily influenced variable within the Control group at 5 years of age, with poorer performance associated with smaller birth head circumference (r_s= -.37, p=.033). Children of mixed ethnicity performed worse than their Black counterparts over language (r_{pb} = -51, p = .001), fine motor (r_{pb}= -.42, p=.012) higher-order adaptive (r_{pb}= -.38, p=.022) abilities and the General Quotient (r_{pb}= -.40, p=.017). No significant correlations emerged between infant variables and any subscales of the FAS/PFAS group at 5 years of age.

Table 18 describes maternal variables associated with developmental outcome as assessed using the GMDS/ER at 5 years of age.

Table 18

Correlations between maternal variables and developmental performance over GMDS/ER subscales at Time 2

GMDS/ER Subscales	Study Group	Maternal Age	Marital Status	Mothers Grade	Employment	Children Alive
	Control	.16†	-.13†	.13†	-.14†	.14†
Locomotor	PAE	-.21†	.12†	.11†	-.00†	-.14
	FAS/PFAS	.34†	.27	.28†	.25	.03
	Control	.19†	-.32†	.39†*	-.33†	.08†
Personal- Social	PAE	-.16†	.03†	.06†	.06†	-.09
	FAS/PFAS	.06†	.41*	.14†	-.17	-.10
	Control	.35†*	-.27†	.33†	-.14†	.24†
Language	PAE	-.16†	.22†	.18†	.05†	-.19
	FAS/PFAS	.24†	.32	.14†	.05	-.13
	Control	.11†	-.25†	.27†	-.34†	.06†
Eye-Hand Coordination	PAE	-.17†	-.08†	.18†	.13†	-.16
	FAS/PFAS	.35†	-.04	.21†	.12	.05
	Control	.09†	-.05†	-.05†	.02†	-.13†
Performance	PAE	-.24†	.12†	.30†*	.23†	-.26
	FAS/PFAS	.30†	.14	-.05†	-.07	.01
	Control	.15†	-.16†	.24†	-.31†	.10†
Practical Reasoning	PAE	-.05†	-.07†	.10†	-.00†	-.13
	FAS/PFAS	.10†	.28	.30†	.02	-.24
	Control	.20†	-.19†	.29†	-.28†	.09†
General Quotient (GQ)	PAE	-.23†	.08†	.25†	.15†	-.22
	FAS/PFAS	.29†	.24	.23†	.06	-.08

Note. Time 1=7-12 months of age, †=missing data, *p <0 .05, ** p <0 .01

Children from the FAS/PFAS group, whose mothers were married, performed better over the Personal–Social (r_s=.41, p=.027) subscale at 5 years of age. Higher levels of maternal education were related to better general achievement over the Performance subscale (r_s=.30, p=.031) of the PAE group, while amongst the Control group similar positive associations were described over social adaptive function subscale (r_s=.39, p = .029). Children from the Control group with older mothers performed significantly better on their language ability (r_s=.35, p=.040).

Finally, Table 19 presents the pregnancy and lifestyle findings, as analysed at 5 years of age, for each group. With age, the later a pregnancy was discovered, the poorer the performance over all but the Personal–Social (r_s= -.44, p=.242) and Practical Reasoning (r_s= -44, p=.232) subscales of the FAS/PFAS group. In addition, the longer mothers breastfed their children from the FAS/PFAS group, the better their gross motor (r_s= .47, p =.015) and practical reasoning outcomes (r_s=.56, p=.003) at 5 years of age. While, a similar positive correlation between length of breastfeeding and developmental outcome on the Practical Reasoning subscale (r_s=.32, p=.020) was identified for the PAE group, the shorter the duration of breastfeeding in the Control group, the poorer their performance over language abilities (r_s=.46, p=.014) at 5 years of age.

While, no significant associations between alcohol and tobacco use prior to and/during the pregnancy of the child of interest, were reported amongst those in the FAS/PFAS group, negative correlations emerged amongst the PAE group over all but the Language (r_s= -.34, p=.018) and Practical Reasoning (r_s= -.26, p=.080) subscales at 5 years.

Table 19

Correlations between maternal lifestyle and pregnancy variables and developmental performance over GMDS/ER subscales at Time 2

GMDS/ER Subscales	Study Group	Month preg	Length Breastfeedi	# of Cig prior preg	# of Cig during preg	Total units of alc prior preg	Total units of alc during preg
	Control	-.14†	-.09†	.21†	.10†	-.18	-
Locomotor	PAE	-.02†	.12†	-.14†	-.19†	-.44†**	-.19†
	FAS/PFAS	-.76†*	.47†*	.09†	.08†	.23†	-.07†
	Control	-.33†	-.20†	.13†	.02†	-.14	-
Personal- Social	PAE	-.14†	.01†	-.09†	-.12†	-.34†*	-.05†
	FAS/PFAS	-.44†	.17†	-.01†	.02†	.07†	.06†
	Control	.09†	-.46†*	.15†	.19†	-.02	-
Language	PAE	-.01†	.18†	-.07†	.03†	-.27†	-.20†
	FAS/PFAS	-.78†*	.27†	.08†	.03†	-.01†	-.26†
	Control	-.37†	-.20†	.02†	.05†	-.12	-
Eye-Hand Coordination	PAE	-.15†	.00†	-.17†	-.22†	-.38†**	-.08†
	FAS/PFAS	-.72†*	.35†	.27†	.20†	.13†	-.08†
	Control	.11†	-.02†	.12†	.19†	.00	-
Performance	PAE	.08†	.04†	-.26†	-.19†	-.34†*	-.04†
	FAS/PFAS	-.76†*	.14†	-.11†	-.12†	-.01†	-.11†
	Control	.02†	-.09†	.19†	.16†	-.10	-
Practical Reasoning	PAE	.31†	.32†*	-.06†	-.08†	-.26†	-.19†
	FAS/PFAS	-.44†	.56†**	.21†	.11†	.01†	-.17†
	Control	-.11†	-.18†	.18†	.11†	-.14	-
General Quotient (GQ)	PAE	.04†	.17†	-.16†	-.15†	-.49†**	-.14†
	FAS/PFAS	-.78†*	.34†	.21†	.13†	.10†	-.20†

Note. Time 1=7-12 months of age, Preg=pregnancy; #=number, Cig=cigarettes, alc=alcohol, †=missing data, *p<0.05, ** p<0.01

4.3 Conclusion

Results presented within this chapter provide both a description of the variable data collected, as well as a presentation of inferential findings required to address the studies research aims and questions. In conclusion, findings from Research Question 1 suggest that infants with FAS/PFAS perform worse than those from both the PAE and Control groups over gross motor and language abilities, assessed using the GMDS with no significant differences between those with some prenatal alcohol exposure (PAE) and the Control group reported during infancy.

At 5 years, when compared to children from the Control group, those with FAS/PFAS, continued to perform poorer, with specific delays emerging between FAS/PFAS and PAE groups over gross and fine motor abilities, as well as skills associated with adaptive reasoning. With age, higher–order ability differences between the PAE and Control groups suggest the impact of low to moderate levels of maternal alcohol consumption.

Furthermore, the consistently poor performance over time by both prenatal alcohol- exposed groups (i.e., FAS/PFAS, PAE groups), suggest that developmental delays may be more related to structural damage, as opposed to environmental harm, providing an example of the nature/nurture debate common in the FASD field. In addition, delays in abilities associated with manual dexterity, manipulation and visual–spatial reasoning, observed in the Control group may suggest domains of the GMDS.ER are more sensitive to environmental influence.

Significant relationships emerged between subscales and the General Quotient (GQ) within both the GMDS and GMDS-ER versions, regardless of prenatal alcohol exposure. During infancy all groups describe associations between subscales as assessed by the GMDS. While trends continue to exist between the subscales at 5 years of age for the FAS/PFAS and Control groups, weak correlations emerge within the PAE group between the Locomotor and Personal–Social; Locomotor and Practical Reasoning and Personal–Social and Language subscales assessed using the GMDS-ER. Furthermore, poor group relationships were described between subscales over versions of the GMDS/ER. By collapsing the sample, significant relationships emerged between the following subscales; Locomotor and Performance; Speech-Hearing and Personal–Social. Findings from Research Question 2 suggest that regardless of prenatal alcohol exposure, children may be using different skills to complete tasks being assessed over time and that underlying constructs assessed by the GMDS and GMDS/ER may differ.

Finally, Research Question 3 presents important findings regarding the associations of infant, maternal, pregnancy and lifestyle variables on early childhood development. While developmental performance of infants with exposure to prenatal alcohol are more likely associated with maternal and/ or pregnancy and lifestyle variables, with age birth anthropometric measurements, the length of breastfeeding impact developmental achievement over groups, regardless of their prenatal alcohol exposure. The following Chapter 5 provides a detailed discussion of the interpretation of these findings with further recommendations and limitations put forth.

Chapter 5 – Discussion and Conclusions

Wisdom is the power to *put our time and our knowledge* to the *proper use*

Thomas. J. Watson

The salient findings are expounded in this chapter with specific reference to the patterns and trends identified from the data analyses. Guided by each research question as derived from the study aims, the following provides a discussion and interpretation of the findings, contextualising them in existing literature.

5.1 Introduction

One of the first longitudinal investigations using both infant and child versions of the GMDS/ER, this study aimed to describe and track early developmental outcomes of children with varying degrees of prenatal alcohol exposure in addition; it included a control group from the same, low socio-economic, postnatal environment. Secondary aims sought to compare performance within groups over domains of the GMDS/ER at two time points, by simultaneously investigating the relationship between infant performance and later achievement at 5 years. Finally, the influence of socio-demographic factors on developmental performance within groups during infancy and again at 5 years of age was considered. This chapter discusses these findings with reference to limitations and recommendations for future studies.

5.2 Developmental differences between groups with varying degrees of prenatal alcohol exposure

As more and more children are diagnosed with learning, attention and behavioural problems, research is turning towards the impact of their prenatal environment. The relationship between prenatal alcohol exposure and structural, cognitive and behavioural abnormalities has been well documented. Considerable research describes the importance of identifying prenatal alcohol exposure as early as possible, but surprisingly little exists regarding early developmental profiles of children with varying degrees of prenatal alcohol exposure (Streissguth et al 1996; Burd et al 2003).

Findings from the current study confirmed significant developmental delays between groups during early childhood development. During infancy, the FAS/PFAS group performed significantly worse than both the PAE and Control groups in terms of gross motor and language abilities. With age, developmental deficits between groups widened across all domains with the exception of language competencies. While language achievement in the Control group increased at 5 years, it worsened for both the FASD and PAE groups. Small differences in effect sizes between groups suggest similar developmental functioning. The FAS/PFAS group continued to perform significantly worse than the Control group over all but language developmental domains with age, with significant differences emerging between the PAE group over gross and fine motor abilities and social adaptive functioning.

While no significant differences between the PAE and Control groups were described during infancy, higher-order cognitive deficits become more apparent at 5 years of age, amongst those

with mild to moderate levels of prenatal alcohol exposure. Findings suggest an association between the amount of alcohol consumed by the mother prior to the pregnancy and an increased likelihood of neurodevelopmental effects during early childhood.

Consistent evidence exists that specific regions of the brain are more vulnerable to the adverse effects of alcohol than others (Mattson et al., 2001; Roebuck et al., 1998; Sulik, 2005). Studies indicate that alcohol related damage to the cerebellum and basal ganglia, are associated with reduced motor coordination ability with children exposed to prenatal alcohol typically performing well on simple gross motor related tasks, but struggling with later more complex motor tasks (Autti–Ramo & Granstrom, 1991; Chandler et al., 1996; Hannigan, et al., 1993; Hannigan & Berman, 2000; Humphriss et al., 2010; Kalberg et al., 2006; Kodituwakku, 2007; Mattson et al., 2011; Valenzuela et al., 2010). Researchers, Jones et al. (1973); Streissguth et al (1994); Jacobson et al. (1993) and O'Leary (2004) all report evidence of similar poor gross and fine motor difficulties amongst infants and children exposed to prenatal alcohol exposure.

Using the Vineland Adaptive Behaviour Scale (VABS), Kalberg et al. (2006) reports that while most of the children in their sample identified with FAS, aged 20–68 months showed significant delays in their gross motor development, significantly more delays were observed across fine motor abilities. In contrast, Adnams et al. (2001) failed to find gross motor differences in alcohol-affected children aged 7 years of age and argued that the Locomotor scale of the GMDS may be insufficiently sensitive in detecting gross motor deficits. Variations in gross motor findings, between studies, may be explained by a difference in ages of the samples. Furthermore, biological mobility is often regarded as the net result of the activity of complex spinal or

brainstem machineries, with motor behaviour one of the best indicators of well-being in the first year of life. Gross motor delays may be more evident during infancy, due to maturation rather than the level of skills involved (Piaget, 1952, McCall, 1981). Converging evidence suggests that regions of the brain which mature first, such as the brain stem and cerebellum, play a critical role in the development of elementary functions; such as, associative learning and reflexive responses (Salman et al., 2006; Kodituwakku et al., 2011). Piaget's sensori-motor phase refers to gross motor skills as being predetermined, elementary abilities used to explore and gain information from the surrounding environment (Piaget, 1952). Thus, findings indicate that general slowness amongst infants with FASD in responding and orientating to stimuli may be secondary, affecting visual processing and subsequent executive functioning (Piaget, 1952; Kable & Coles, 2004; Stanton & Goodlet, 1998). While the current study confirmed the presence of gross motor delay at 5 years of age in the FAS/PFAS group, findings may have been influenced by the use of the revised version of the GMDS-ER which could be more sensitive than the older version of this scale in detecting these gross motor difficulties (Luiz et al., 2004). Barr et al. (1990) reported both fine and gross motor delay amongst 4-year old children, moderately exposed to prenatal alcohol exposure. Corroborating Barr's conclusions, the current study found similar poor gross motor performance during infancy and at 5 years of age. While both studies describe moderate levels of prenatal alcohol use, the current study includes two further groups namely, heavy alcohol use and non-drinkers.

While differences in motor development are less important in the overall diagnostic criteria for FASD, Kalberg et al. (2006) suggests that this area may become one of interest, especially when confirming an early diagnosis and in understanding the overall development of children exposed

to alcohol. Evidence suggests that when impaired, these basic motor functions influence the development of subsequent higher-order skills (Herbert et al., 2003; Salman et al., 2006; Vygotsky, 1978, 1986). Early gross motor deficits affect the developing child's ability to explore and learn about his world, thus affecting his subsequent cognitive development (Piaget, 1952; 1963). These findings concur with previous findings that developmental motor delays in children with FAS often parallel cognitive delays (Osborn et al., 1993). Although the current study was able to confirm gross motor deficits amongst children diagnosed with FAS/PFAS over time, it did not find significant fine motor delays during infancy amongst the same group, with significant lags only emerging at 5 years of age. In contrast, Van der Leeden and colleagues (2001) were able to report poor fine motor development amongst infants of 7 months of age using a neurological examination. A possible explanation for fine motor differences found at 5 years of age but not during infancy may lie in the possibility that the Eye Hand Coordination subscale of the Infant Version of the GMDS may be less sensitive to detecting fine motor deficits, especially amongst prenatal alcohol exposed infants than the version of the GMDS/ER for older children.

Due to the holistic nature of childhood development, it is accepted that developmental domains are interrelated and that similar correlated constructs may be assessed across domains, especially during infancy when motor ability forms an important developmental milestone. According to Griffiths, each subscale of the GMDS was devised to be used individually or collectively where necessary (Griffiths, 1970; 1984). Consequently, the Eye Hand coordination subscale could be used in conjunction with the Locomotor subscale to obtain a clearer picture of the child's motor abilities including gross motor skills, such as crawling and walking; manipulative skills, fine

motor skills such as playing with or co-ordinating blocks and stability skills of balance and control (Gallahue & Ozmann, 1995; Griffiths, 1970; 1984; Matney, 1999).

The absence of significant differences during infancy between the PAE and Control groups in areas of development, suggests there may be no effect or too little effect to be detectable due to the current samples size. Alternatively, findings may describe the considerable variability in the PAE group with the effects of prenatal alcohol exposure dependant on the time during pregnancy when alcohol was consumed. It is known, due to teratogenic central nervous system (CNS) damage, children with some prenatal alcohol exposure may not present with all the classic FAS features but neurodevelopmental deficits, especially in higher-order cognitive domains may become more evident as the child develops (Connor et al., 2000; Kodituwakku et al., 2001; Mattson et al., 1999; Stratton et al., 1996; Willford et al., 2004). Given the marked individual differences in maternal alcohol metabolism, functional and developmental deficits are likely. Previous studies have confirmed the relationship between the dose of alcohol and observed effects on structural brain abnormalities, as being critical with developmental outcomes dependent on various factors such as; the quantity, frequency and timing of the alcohol exposure (Autti-Ramo & Granstom, 1991; Larroque et al., 1995; McCarver, 2001; Streissguth et al., 1986). While the timing of maternal alcohol consumption was not recorded in the current study, it may explain the lack of significant developmental differences, especially during infancy, between the PAE and Control groups.

While increases in the various assessed developmental domains were found between infancy and 5 years of age amongst children with no alcohol exposure, results relating to the FAS/PFAS and

PAE groups tentatively suggest decreases in higher-order cognitive abilities, as assessed by the language, fine motor and performance subscales of the GMDS-ER at 5 years. Similar findings have been described amongst samples of poorly resourced communities. Similar higher-order delays were described in both the FAS/PFAS and PAE groups when compared to the Control group. Findings suggest that mild to moderate levels of prenatal alcohol exposure combined with environmental factors have more damaging effects on executive, cognitive development than purely environmental variables. Another explanation may be that while the GMDS is able to identify deficits associated with heavy alcohol use during infancy, it proves less sensitive in detecting subtler delays resulting from mild to moderate prenatal alcohol exposure.

While children with FAS/PFAS from the current study continued to perform significantly worse than the PAE and Control groups in terms of motor ability, with age, further developmental differences became apparent over higher-order constructs (namely the Performance and Practical Reasoning subscales). At 5 years of age, alcohol exposed children, i.e. those in the FAS/PFAS and PAE groups, obtained significantly lower scores on the Performance and Practical Reasoning subscales of the GMDS-ER when compared to their non-exposed counterparts. As both these subscales provide good estimates of higher-order processes involved in logical reasoning and executive functioning, these findings concur with existing evidence of significant impairments in problem solving abilities, abstract thinking, planning and cognitive flexibility amongst children with heavy prenatal alcohol exposure (Adnams et al., 2001; Coles et al., 1992; Kerns et al., 1997; Kodituwakku et al., 2001; Mattson, et al., 1999; Streissguth et al., 1994). A poor performance on the Practical Reasoning subscale, if associated with a low score on the Performance subscale may further indicate that the child has developmental delay, a possible

precursor to intellectual disability, with serious educational implications (Luiz et al., 2004). Findings support the notion that with age, as task demands become cognitively more demanding, the FAS/PFAS and PAE groups find them more challenging when compared to their non-exposed counterparts (Kodituwakku et al, 2011).

It is encouraging that the current findings on the GMDS-ER at 5 years of age parallel those of previous research on executive functioning and visual-spatial processing in children with prenatal alcohol exposure (Connor et al., 2000; Kerns et al., 1997; Kodituwakku, et al., 2001; Mattson et al., 1999; Rasmussen, 2005). With poor executive functions observed in both groups exposed to prenatal alcohol it seems likely that these significant delays may well be related to their exposure to alcohol in utero. This statement, however, is made with caution as no causal conclusions could be reached due to the correlational design of the study. Furthermore, various research describes the influence of external contributory factors, such as infant anthropometric measurements, maternal age, level of educational and nutritional status to name a few, as contributors to development of the child (Baker–Henningham et al., 2003; Bradley & Corwyn, 2002; Brooks–Gunn & Duncan, 1997; Brooks-Gunn et al., 1996; Brooks-Gunn, Guo & Furstenberg, 1993; Chetty, 2012; Cockcroft et al., 2008; Ensminger & Fothergill, 2003; Gale et al., 2006; Grantham–McGregor, et al., 2007; Hack, Klein & Taylor, 1995; Hamadani & Grantham–McGregor, 2004; Kirksey & Wachs, 1994; Lalloo, 1997; Mistry et al., 2004; Richards et al., 2002; Shenkin, Starr & Deary, 2004; Short, 1987; Silva et al., 2006; Sirin, 2005). It is important to consider this even when dealing with prenatal alcohol exposed groups. The impact of external factors on childhood development will be discussed in more detail in section 5.4. The findings from the current study provide further important insights into identifying delays in

abilities associated with attention, skill in manipulation, visual-spatial reasoning, problem solving and concept formation, all which underpin aspects of later executive functioning. While the Extended Version of the GMDS-ER is able to evaluate some aspects of executive function, it is not a specialist executive functioning test and it is suggested that further, more detailed assessments of executive functioning should be used in future studies. Deficits in executive functioning translate directly into dysfunctional behaviour and problems with daily functioning, as well as academic and later occupational functioning (Kelly et al., 2000; Kodituwakku et al., 2001; Schonfield et al., 2006; Steinhausen, 1995; Streissguth et al., 1991; Whaley et al., 2001).

While the PAE group performed slightly below that of the Control group on adaptive skills, the FAS/PFAS group generally demonstrated significantly lower scores as both infants and at 5 years. In contrast, Coles et al. (1991) found alcohol–exposed children to be comparable to controls in terms of their adaptive skills. Similarly, Adnams and colleagues (2001) reported no adaptive skill deficits in children aged 7 years with FAS and suggested that the Personal-Social subscale of the GMDS may be less discriminating of these skills in the FAS child, when compared to other subscales. While evidence suggests that poor maternal care during the first few years of life may result in social deficits, affecting bonding and attachment, it seems in some cases such deficits amongst alcohol exposed individuals may largely be exacerbated by the alcohol insult on specific regions of the brain (Bowlby, 2000; Kelly et al., 2000). Lack of significant differences may in part be due to the less objective nature of the Adaptive subscale–especially in the Infant Version (Huntley, 1996).

Many of the afore-mentioned studies comprise samples that vary in age, levels of prenatal alcohol exposure and tests administered to the current study, as well as to each other. However,

they do support the idea that delayed cognitive processes, associated with prenatal alcohol exposure contribute to difficulties across various domains of developmental, as well as later academic skill. In a recent review, Kodituwakku and colleagues (2011) propose that if prenatal alcohol exposure leads to structural brain damage, then irregular profiles relating to both visual-spatial (higher–order executive abilities) and verbal (cognitive) deficits would be expected in such children. The development of language provides important evidence of central nervous system (CNS) integrity and remains an important milestone for children, as well as a good indicator of overall development (Coplan et al., 1998). With language and thinking interrelated, it is not surprising that speech and language acquisition are particularly sensitive to various neurodevelopmental insults including those associated with neurological and oral-motor impairment, hearing loss and general cognitive delay (Piaget, 1952; 1963).

Few studies have examined the language skills of children with varying degrees of prenatal alcohol exposure, with those that have demonstrating highly variable results. Studies of children with substantial prenatal alcohol exposure all report marked deficits in language development, including expressive and receptive abilities, naming, word comprehension, grammar, semantics and pragmatics (Abkarian, 1992; Becker et al., 1990; Carney & Chermak, 1991; Conry, 1990; Janzen et al., 1995; Mattson & Riley, 1998; Mattson et al., 1997). Poor language abilities in all groups were found in by the current study. Infants from the FAS/PFAS and PAE groups performed well below average with those from the Control group performing slightly below average. With age the language abilities of the Control group increased, with those in the group associated with prenatal alcohol exposure decreasing and remaining below average. This may suggest that either language ability within this community is poor and/or that the GMDS/ER is

unable to differentiate between the more obvious languages differences associated with prenatal alcohol exposed groups.

The current study found substantial differences between groups in terms of language ability, during infancy, with differences reported at 5 years of age between the FAS/PFAS and Control groups. Similar results were reported by Fried and colleagues (1988, 1990 &1992) with significant associations between prenatal alcohol exposure and language delay at 13 months, 2 and 3 years of age but not at 4-years of age (Fried & Watkinson, 1988; Fried & Watkinson, 1990 & Fried, O'Connell & Watkinson, 1992). Coles and colleagues also failed to find any association between alcohol exposure and the language ability of a group of children aged 5 years 10 months, suggesting that language skills may be more preserved than skills associated with visual spatial ability (Coles et al., 1991).

In contrast, McGee et al. (2009) describe marked deficits in both expressive and receptive language abilities, amongst preschool children, aged 3–5 years with heavy prenatal alcohol exposure, using the Clinical Evaluation of Language Fundamentals, Preschool version (CELF-P). Using the GMDS, Adnams et al. (2001) further describe poor language performance of 35 South African children with FAS at 7 years of age, as being highly distinguished from a matched control group. Differences in verbal findings between the current and afore-mentioned studies may be explained by the measurements used and the age of the samples. The CELF-P may be more sensitive in detecting language deficits in children younger than 5 years of age, while the GMDS seems able to do so at 7 years of age (Adnams et al., 2001; McGee et al., 2009). Another possible explanation for the current study's language findings may relate to the comparison of

verbal skills over various age groups. According to the natural progression of language development, items assessed by the GMDS/ER vary depending on the age of the child. In the first year, infants are assessed according to their use of words, through labelling objects with a definite meaning such as “mama, dada”. With age, speech develops with an increase in vocabulary; by the fifth year, the child is being assessed on their usage of descriptive words, understanding of opposites and ability to describe the function objects (Griffiths, 1970, 1984; Luiz et al., 2004). While the reported low correlations obtained between versions of the GMDS/ER over time are discussed in more detail in section 5.3, this may offer a possible explanation for language findings from the current study suggesting a limitation in the methodology of the study rather than a specific developmental difference. Developed to focus on a child’s pace of attaining age–appropriate developmental skills, the GMDS/ER may also be less suited to evaluating specific domains of dysfunction. Overtime, furthermore, while capable of detecting developmental deficits associated with heavy prenatal alcohol exposure, at both time points, the GMDS/ER may be less sensitive in distinguishing those associated with lower levels of alcohol, especially during infancy.

A possible explanation for the significant differences at 5 years of age but not during infancy over higher-order cognitive abilities of alcohol-exposed groups may be that the Infant version of the GMDS is not sensitive enough in detecting higher-order cognitive abilities during infancy. Alternatively, from a biological perspective the immaturity of an infant’s higher-order cognitive abilities may restrict the ability of assessing such constructs prior to their emergence (Piaget, 1963).

Explanations for the diverse findings between research studies include variations in their methodologies, subject characteristics, sample sizes, age ranges, and varying assessment tools and in some cases, the lack of comparison groups (Kodituwakku, et al., 2011; McGee et al., 2009). Furthermore, the variable nature of the effect of prenatal alcohol exposure is likely to determine the level of structural damage to specific brain regions, contributing to variations in developmental outcomes. While the current study compared groups with varying degrees of prenatal alcohol exposure, other studies only included children with lower levels of exposure (but diagnosed as Non-FASD) (Fried et al., 1988, 1990, 1992).

5.3 Relationship between infant performance and later achievement over developmental subscales of the GMDS/ER

The latent variable of child development is difficult to measure, especially over time. Confidence that a developmental test's ability to measure the same functional skills over time is essential, yet to date no studies have examined subscale correlations between the Infant and Extended versions of the GMDS/ER an advantage afforded by the longitudinal study reported in this thesis.

While a number of studies have focused on the neurocognitive profiles of children with FASD during school-going age (Adnams et al., 2001; May et al., 2000; May et al., 2008; Urban et al., 2008; Viljoen et al., 2005), few have addressed the developmental profiles of such children, during infancy and early childhood using the GMDS/ER. Findings from the current study indicate that regardless of prenatal alcohol exposure, no significant correlations emerged between subscales of the Infant and Child versions of the GMDS/ER over time. This suggests that subscales used to assess development in infancy are possibly measuring different constructs to those being used at 5 years of age. Due to the limited availability of research relating to the correlations between versions of the GMDS/ER, it proves difficult to compare our findings to

other studies. As the lack of correlations is true for all groups in the present study, it confirms findings have more to do with the instrument and constructs being measured, and less to do with prenatal alcohol exposure.

These findings concur with those of Luiz et al. (2006) who similarly described the evolving nature of childhood in which they sought to identify the underlying dimensions tapped by subscales of the GMDS/ER in a sample of 180 South African children aged between 5 and 7 years of age. Their findings confirm that more discrete, cognitive, motor and personal–social functions being tapped by the subscales are less clearly delineated; possibly suggesting various aspects of the constructs being tapped over different years. Luiz et al. (2006) stressed that their findings may point to the structure of the GMDS/ER in that items are placed in order of difficulty for each year. Similarly, this may prove an important contributor in the present study. While the Luiz et al. (2006) study differs to the current studies in regard to the ages of children, it stands to reason that if constructs being assessed in their study between 5 and 7 years of age differ, then similar findings would be expected between infancy and 5 years of age, when developmental progression is greater. Another difference between the current study and that of the afore-mentioned by Luiz et al (2006) was their use of the revised version of the GMDS-ER, where the current study used both the Infant version of the GMDS and the Revised Version of the GMDS, which may have further influenced the findings. Furthermore, while the current study included children from more rural, impoverished communities with varying developmental histories, due to prenatal alcohol exposure, the Luiz et al. (2006) study assessed children from urban areas considered to have had a normal birth and developmental trajectory. By implication, findings from the current study make it difficult to draw longitudinal conclusions regarding the

early childhood development of groups, with different constructs being assessed at different ages, using both versions of the GMDS/ER. Possible reasons for the current study's findings may in part be due to the small group sizes and/or the presence of outliers, known to influence correlational analysis (Field, 2009).

While not a main aim of the study, groups were collapsed, in an attempt to increase the sample size and thus the ability to detect an association between developmental constructs over versions of the GMDS/ER. The only significant association suggested that the better an infant's gross motor ability assessed by the Infant Version of the GMDS, the higher their score at 5 years of age over the Performance subscale on the GMDS/ER, measuring manipulation skills. The nature of the Performance subscale of the GMDS-ER at 5 years of age includes items, which assess size discrimination, form perception, manual dexterity, construction with memory and visual spatial reasoning (Luiz et al., 2004). At 5 years of age, both the Fine Motor subscale and Performance subscale of the GMDS/ER require the child to demonstrate their ability to carry out a range of fine motor tasks (Luiz et al., 2004). In order to do so the child would need to possess a level of spatial and visual perception appropriate for his age, developmental constructs which form the foundations during early gross and fine motor development. Previous research suggests an association between basic sensori–motor functions and later more sophisticated higher-order executive functions, which may explain a possible reason for the current study's findings (Herbert et al., 2003; Salman et al., 2006; Vygotsky, 1978, 1986). Another finding from the current study describes a positive association at 5 years of age, between social adaptive functioning and infant language ability. Items of the Personal-Social subscale of the GMDS-ER at 5 years of age assess the child's proficiency in daily living activities, his level of independence

and ability to interact with other children. A number of items are language based such as: "Are you a boy or a girl?"; "How old are you?"; "What is your family name"? It makes sense then that children with speech and language delay may not accurately be able to answer these questions; hence it is not surprising that a link between early language ability and later performance over the social adaptive functioning subscale of the GMDS–ER is evident.

Finally, findings from the current study suggest a relationship between general infant ability measured by the general quotient (GQ) and later performance over social adaptive functioning, fine motor ability and manipulation constructs assessed at 5 years of age, across groups. As the general quotient (GQ) is calculated by combining subscale scores, it is obvious that it would be correlated with each subscale within the same version (Luiz et al., 2006; Griffiths, 1970). As part of the standardisation procedure, Griffiths (1970) studied the interrelationships between subscales and the General Quotient (GQ) of 285 British children in their fifth year and similarly described correlations between all subscales, thereby confirming internal consistency of each version. Given the nature of the constructs identified at 5 years of age, it is possible that the Infant version of the GMDS is capable of identifying later more specific, higher-order cognitive abilities. Alternatively, it may suggest that the GMDS-ER at 5 years of age is more sensitive to variations associated with language, manipulation and social adaptive functioning.
What is evident is that subscales over versions of the GMDS/ER tap more than one construct. While Griffiths (1970) supports that each subscale measures only one prospect of development, These findings concur with those of Luiz et al. (2006) in which they examine underlying dimensions tapped between subscales within the GMDS-ER, in a sample of 180 children aged between 5 and 7 years of age. Furthermore, they similarly confirm the evolving nature of

childhood development, in which aspects of the construct being tapped differ over different years (Luiz et al., 2006).

No other studies appear to have described the longitudinal relationship between subscales over versions of the GMDS/ER. Possible explanations may suggest that findings had been influenced by the structure formation of the measures, in that items within each subscale were placed in an increasing order of difficulty, within each conceptual year (Luiz et al., 2006). Secondly, direct comparisons between versions of the GMDS/ER are likely to be prone to misinterpretation due to the difference in means and standard deviations of the instrument (Ivens & Martin, 2002). It was hoped that using converted *z*-scores for both versions of the GMDS/ER in the current study would help overcome some potential misinterpretation errors.

Another reason for a non-significant correlation between versions of the GMDS/ER may be the reduced retest reliability for the infant version. Researchers report low test-retest reliability for infants under a year of age, with higher reliability existing from the second year onwards, suggesting a weakness in the longitudinal nature of the instrument (Huntley, 1996; Knoesen, 2003, 2005; Kotras, 2001, 2003; Luiz, 1988a, 1988b, 1988c, 2006; Laughton et al., 2010; Luiz et al., 2004; 2006, 2001). In a study describing the developmental profile of infants from a low socio-economic background in South Africa, Laughton and colleagues (2010) compared the GMDS scores obtained at 10–12 months to those at 20–22months. Scores of the thirty-one infants in the group were within average limits at 11 months, and other than Locomotor, decreased significantly in their second year of life, with Language most affected. They conclude that while the GMDS is a valuable tool of assessment for young South African children it may

over-estimate infant abilities in the first year of life, especially amongst children in deprived settings.

While not completely surprising, given the structural differences in the central nervous system (CNS) between age groups, the lack of significant correlations between subscales of the GMDS/ER from infancy to childhood in the current study may suggest the use of different skills to complete tasks at different age groups. As the GMDS is generally used as a tool to measure skills and their development from birth to 8 years of age, poor correlations between versions is concerning. The absence of overlap in abilities found in our study, between versions of the GMDS/ER, suggests certain infant skills may relate to later performance over cognitive and social adaptive subscales.

It is impossible to know whether the lack of correlation found represents the influence of confounding environmental factors. Experts in teratology emphasise the importance of considering relevant covariates in examining the effects of prenatal alcohol exposure during early childhood, with studies describing how risk factors often co-occur and interfere with children's development (Engle et al., 2007). A question asked in the present study was which socio-demographic variables were most strongly associated with developmental achievement during early childhood amongst groups with varying degrees of prenatal alcohol exposure and a Control group from the same community. The following section describes the relationships between the identified variables and the interdependent subscales of sensory–motor, cognitive–language and social–emotional functions, assessed by the GMDS/ER.

5.4 Impact of socio-demographic variables on early childhood development

Unfortunately most assessments of development over time are influenced by the child's environmental experience. Results from the current study indicate that a complex set of variables are at play, each of which alone could have negative impacts on the developing child, yet in combination, their efforts are compounded, making it almost impossible to separate them out. Associations between socio-demographic variables and early childhood development identified in the current study are discussed under the following sections: infant, maternal and pregnancy, lifestyle characteristics.

5.4.1 Infant characteristics.

It is clear from the significant correlations in the present study that several infant demographic variables were associated with poor developmental outcomes during early childhood, although more were anticipated. The fine motor ability of male infants from the Control group in the current study emerged as poorer than those of female infants. These findings are consistent with other developmental studies suggesting that while boys' gross motor and spatial memory skills generally develop at a slightly faster pace than girls' do, they are slower at developing language and fine motor skills (Arcenaux et al., 1996; Born et al., 1987; Blakemore et al., 2009; Halpern, 2000; Maccoby & Jacklin, 1974; Reinisch & Sanders, 1992). Findings suggest that the time and rate of development of certain areas of the brain, associated with language, spatial memory, motor coordination and social adaptive functioning may vary according to gender, influencing developmental abilities (Hanlon, Thatcher & Cline, 1999).

The current study did not find similar gender differences within alcohol-exposed groups. These findings compare to previous studies, which similarly report no gender associations, based on prenatal alcohol exposure (Mick et al., 2002). In contrast, animal studies have demonstrated

gender differences in the effects of prenatal alcohol exposure on responsiveness to stress, suggesting greater vulnerability among female offspring (Weinberg, 1992). In a study conducted by Rasmussen, Horne and Witol (2006), significant associations between gender and executive functioning abilities were reported with girls rated as having more executive functioning difficulties than boys at 9.5 years of age. As they used the Behavioural Rating Inventory of Executive Function (BRIEF), they suggest this finding may reflect a bias among parents of girls or it may well be that girls with FASD display more serious deficits in executive functioning than boys. In other studies, girls were more likely to demonstrate mental health problems between ages 4 and 8 years (Kapil et al., 2007), while boys aged 6-16 years with FASD were more likely to be diagnosed with ADHD than girls with the same diagnosis (Herman et al., 2008). Findings associated with gender differences amongst groups with prenatal alcohol exposure are limited and inconsistent in their results and outcome measures, future studies are needed in this regard. The lack of gender associations described in the current study may further be explained by the gender ratio of the sample.

An unexpected finding describes the impact of ethnicity of non–exposed children, over language, eye hand coordination, concept formation and problem solving abilities at 5 years of age with those of mixed ethnicity performing worse when compared to their Black counterparts. Similar significant differences were described in a study within and between black, coloured, white and indian children, aged 5 years of age (Allan, 1992; Bhamjee, 1991; Luiz et al., 2001). While findings from the current study are relevant, they do not necessarily suggest cultural differences over specific subscales and may provide more valuable information based on the impact of other socio-demographic factors such as smoking, violence or types of deprivation associated with a

longer history of acculturation, due to the history of colonisation and slavery. Findings may also be explained by the unequal proportions of mixed ethnic and black participants within the sample. Groups were not matched according to ethnicity, with more mixed ancestry children found in the alcohol-exposed groups. This in itself is an important finding. Although an emerging, slightly controversial field transgenerational epigenetic studies describes significant correlations between environmental exposures at critical periods and cross-generational outcomes of alcohol exposure, which may explain some of the ethnic developmental differences described in the current study (Bygren, Kaati & Edunsson, 2001; Pembrey et al., 2006). Future studies are needed to explore this. Findings from the current study indicate that while differences between groups are less obvious during infancy, they emerge as more evident at 5 years of age, particularly over complex, higher-order functions.

Decreased birth weight, height and head circumferences in developing countries have been associated with poor maternal nutrition and further constraints in fetal nutrition, impacting early brain development and later functional development in adulthood (Brown & Pollitt, 1996; Fattal–Valevski et al., 1999; Grantham–McGregor & Fernald, 1997). It is clear from the present study that birth measurements influence developmental ability at 5 years of age over gross and fine motor, adaptive functioning, manipulation and speed abilities, amongst children with mild to moderate levels of alcohol exposure (PAE group) with a possible effect of small fetal size related to alcohol exposure. Children from the PAE group, with larger head sizes at birth, performed better over language abilities at 5 years of age. Similarly, those from the Control group with smaller head measurements performed poorly. In summary, children with better birth anthropometrics performed better when compared to those with smaller measurements.

Findings suggest that developmental performance is influenced by prenatal environmental or genetic factors that determine both head size at birth and postnatal growth. In at least one cohort of a South African study, maternal head circumference of FAS children was significantly smaller than the comparison group (May et al., 2005) which may indicate mothers of FAS/PFAS children may themselves have FAS/PFAS. While measurements of maternal head circumference were not reported in the current study, it is important to consider their link to infant head circumference as a possible explanation for decreased performance during early childhood. Findings from the current study suggest language abilities of children aged 5 years of age with no prenatal alcohol exposure, assessed using the GMDS/ER are likely associated with head circumference measurements at birth. While birth head circumference does not emerge as being significant amongst groups with FAS/PFAS in the current study, research indicates that children diagnosed with FASD are more likely to present with smaller head circumferences. This suggests that head circumference remains an important feature when making the FAS/PFAS diagnosis (Hoyme et al., 2005; Naidoo et al., 2005; O'Leary, 2004; Riley et al., 1995; Urban et al., 2008; Viljoen et al., 2005). The relationship between maternal substance use and physical development, seen as general growth delay, smaller head size and lower birth weight has been well researched, with links between physical development and poorer developmental outcomes and lower IQs evident (Coles et al., 1992; Mills et al., 1984; Streissguth et al., 1985). While many previous studies examining the impact of birth measurements failed to consider prenatal alcohol exposure, the current study adds to existing literature by suggesting that regardless of mild to moderate levels of prenatal alcohol exposure, infants with better birth measurements performed better over specific developmental abilities.

Findings from the present study further describe specific protective variables, such as duration of breastfeeding and birth measurements both associated with intrauterine and postnatal infant nutrition, as being related to better developmental performance at 5 years of age amongst children exposed to mild-moderate levels of prenatal alcohol. Regardless of prenatal alcohol exposure, birth measurements remain useful, even at 5 years of age, in the identification of the period during which malnutrition occurred. Evidence from animal research suggests a complex interplay of early under–nutrition, iron-deficiency, environmental toxins, stress, poor stimulation and the quality of the environment which modify the structure's and functions of brain regions with subsequent lasting effects (Brown & Pollitt, 1996). Earlier animal investigations revealed paternal alcohol use is associated with low birth weight and cognitive and behavioural delays, very few recent studies have confirmed these findings, suggesting the speculative nature of this line of research (Cicero, 1994; Hegedus et al., 1984; Little & Sing, 1987). While paternal alcohol use was not described in the present study, high rates of alcohol use have been reported in the community and may serve to explain decreased performance over all groups in the current sample (Parry, 1998).

In contrast to previous research, no evidence was found in the current study of significant association between maternal smoking and poor developmental performance during infancy (Bove et al., 2002; Martin, Dombrowski, Mullis, Wisenbaker, J & Huttunen, 2006). However, with 48% of mothers from the current sample confirming smoking during pregnancy, findings compare to previous studies describing the interaction between smoking, drinking and evidence of increased risk of preterm labour, low birth weight and growth restrictions (Odendaal et al., 2009).

5.4.2 Maternal characteristics.

Results from the current study suggest that specific maternal variables, particularly those associated with socio-economic status (SES) are linked to deficits in development during early childhood. Although specific income indicators were not collected in the current study, maternal level of education and occupation are generally well correlated and good estimates of income (Ensminger & Fothergill, 2003; Sirin, 2005). Maternal education emerged, in the current study, as being negatively associated with fine motor performance during infancy amongst the PAE group. With age, further positive associations were found over the Performance subscale, representing higher-order cognitive abilities. Similarly, higher levels of maternal education in the Control group indicated improved fine motor and social adaptive functioning abilities at 5 years of age. Maternal unemployment emerged as being negatively associated with language abilities during infancy in the PAE group. However, with age, maternal unemployment was linked to better performance over social adaptive functioning abilities. This may suggest that while mothers from the PAE group are unemployed, the stimulation and time spent with their children before 5 years of age, has a positive effect on their ability to interact and engage with others.

Findings from a study conducted on 40 Black South African infants age between 13 and 16 months of age, similarly indicate that children of lower socio-economic status (SES) performed significantly worse than more affluent counterparts (Cockcroft et al., 2008). Infants with less educated, non–professional mothers performed significantly worse in terms of their gross motor functioning. While the current study obtained similar findings related to maternal education and occupation, differences emerged over the identified developmental subscales, with deficits reported in terms of fine motor deficits and language, in contrast to those of gross motor delay

identified by Cockcroft et al (2008). These differences may be explained by exposure to prenatal alcohol, with families that abuse substances frequently characterised by socio-economic challenges, antisocial behaviour and other drug use (Hussong et al., 2010).

It is well established that socio-economic status (SES) itself strongly influences childhood cognitive functions, with research amongst infants as young as 6 months, supporting the detrimental effects of poverty (Gale et al., 2006; Hack et al., 1995; Richards et al., 2002; Shenkin et al., 2004; Silva et al., 2006). In reality, a number of other factors, such as inadequate food, poor sanitation and hygiene are often directly related to poor maternal education, increased maternal stress and depression, larger family sizes and inadequate stimulation (Baker–Henningham et al., 2003; Bradley & Corwyn, 2002; Brooks–Gunn & Duncan, 1997; Brooks-Gunn et al., 1993; Grantham–McGregor, et al., 2007; Hamadani & Grantham–McGregor, 2004; Kirksey & Wachs, 1994; Mistry et al., 2004). Research suggests that children who come from impoverished homes with unemployed parents, with limited education do less well on intellectual assessments and school performance than children from more privileged homes (Lalloo, 1997; Short, 1987). Poverty is associated with higher fertility levels and larger household sizes (Grantham-McGregor, 2007). Large sections of the South African population suffer from poverty and are disadvantaged, in poorly resourced communities, and at particular risk to poor cognitive development. In the current study, the more children in the family, the poorer children from the Control group were likely to do on measures of language and manipulation abilities during infancy. However, children aged 5 years of age from the FAS/PFAS group, whose mothers were married were more likely to perform better over social adaptive functioning. These findings may go some way in explaining the association between the

quality of the home environment, maternal health and the child's relationship with the caregiver (shown to influence levels of stimulation and later developmental ability) (Bowlby, 2000; Grantham–McGregor et al., 2007). While mother-infant interactions were not measured in this study, typically severe economic constraints and increased family size significantly reduce the quality and quantity of parenting due to both financial and psychological stress. The fact that the performance of the PAE group followed that of the Control group at 7 months but moved closer to the FAS/PFAS group at 5 years could suggest structural prenatal damage becomes more evident with age or it could be reflective of the complexity of development. Due to less exposure to prenatal alcohol, the PAE group showed more structural potential at birth when compared to the FAS/PFAS group, but may have missed key developmental milestones due to poor parenting/stimulation considering mothers from this group used alcohol more frequently than the Control group. In some cases the use of alcohol may directly be related to the quality of parenting, while in other cases the influence of maternal alcohol use could have been mediated by protective relationships with other adults/children. The influence of poor parenting would not have been as apparent in the FAS group as their performance, even with detrimental environments, would have remained poor. Children with FASD are more likely to live in homes with family instability, dysfunction, and foster care, all of which have been known to intensify intellectual and social delays amongst children with non FASD (Abkarian, 1992). An early diagnosis and a stable nurturing home have been described by researchers as amongst the strongest protective factors against the development of secondary disabilities (such as disrupted school experiences and trouble with the law) (Streissguth et al., 1994). It seems that while maternal socio-economic factors influence infant demographics, when they co-occur with prenatal alcohol exposure, they cause devastating deviations to overall childhood development.

Given the reported high prevalence rates of alcohol exposed pregnancies in South Africa, studies investigating maternal risk factors of having a child with FAS/PFAS confirm that these mothers are more likely to be older, live in rural impoverished areas, have lower levels of education, be unmarried, have more children, smoke tobacco and suffer from poor nutrition with low body mass indices (BMI) (May et al., 2005; May et al., 2008; Urban, et al., 2008). Other findings included higher levels of depression and living with a partner with a drinking problem (May et al., 2008; Urban et al., et al., 2008; Chetty, 2012).

While the current study confirmed these findings, it did not identify significant associations between maternal demographic variables and developmental performance in the FAS/PFAS group. A possible reason for this may be that the effect of heavy prenatal alcohol exposure, in the FAS/PFAS group, overwhelmed the effect of other maternal demographic variables. Alternatively, it may indicate the insufficient variance in the variables of the FAS/PFAS group, as well as the size of the sample being too small.

5.4.3 Pregnancy and lifestyle characteristics.

While most mothers change their lifestyles and abstain from alcohol following the confirmation of their pregnancy, some continue to drink low to moderate amounts throughout (Henderson et al., 2007). It is clear from the current study that pregnancy recognition directly influenced developmental abilities during early childhood development. Infants from the FAS/PFAS group whose mothers confirmed their pregnancy later, performed poorly over language and adaptive functioning tasks. Similar, deficits associated with fine motor abilities were described in the Control group, amongst infants whose mothers recognised their pregnancies later. At 5 years of age, decreased performance over gross and fine motor abilities, adaptive functioning,

manipulation and speed abilities were associated with later pregnancy recognition in the FAS/PFAS group

It seems likely that the later a pregnancy was recognised, the longer mothers might have used alcohol, influencing early fetal development of critical brain regions (O'Connor et al., 2011). While many women reported that they had stopped drinking at their pregnancy recognition, on average women in the sample were unaware they were pregnant until 3.7 months of gestation, suggesting a longer period of fetal alcohol exposure. Similar findings were described by O'Connor et al. (2012) in which they describe pregnancy recognition in their sample at the 9th week of gestation, with mothers from a similar community in South Africa, engaging in heavy patterns of alcohol consumption (≥3 drinks per occasion). The current study confirms the impact of early prenatal alcohol exposure with significant negative associations between units of alcohol consumed prior to the recognition of the pregnancy in the PAE group and similar developmental deficits over all but the language subscale at 5 years of age.

While every effort was taken in the current study to ensure mothers from the Control group were non-drinkers prior to and/or during pregnancy, some may still have consumed low levels of alcohol prior to the confirmation of the pregnancy thus influencing the developmental performance of the child of interest. Previous research indicates that between 15–50% of foetuses are exposed to low levels of alcohol in utero (Ebrahim et al., 1998, Floyd et al., 1999a, b). The current study's findings raise concerns as to the reason for the later recognition of pregnancy amongst women in the current sample. While body mass indices (BMI) were not included in the current sample, previous studies show that mothers of FAS/PFAS children typically have lower BMIs than controls (Khaole et al., 2004; Urban et al., 2008). Researchers

are unsure as to whether these findings are due to heavy drinking or malnutrition, with the two very much linked. However, with 29% of the children in the present sample showing signs of being underweight (less than 2.5kg at birth), findings from the current study suggest that the sample is far from "normal" and cautions against the generalizability of birth anthropometric findings from more normal populations. Typically, underweight babies generally indicate underweight mothers (De Onis et al., 1998; Walker et al., 2007). Alternatively, findings may confirm high rates of unplanned pregnancies in poorly resourced communities such as those of the present samples. While these interpretations are speculative, they provide important implications for early preventative care and policy development aimed at women of childbearing age, pre-conception. Findings from a recent study report that 1 in 5 women from rural communities were at risk of having an alcohol-exposed pregnancy (AEP), by virtue of current alcohol use, being fertile, not pregnant and not using effective contraception (Morojele et al., 2010).

While prenatal nutrition is important, postnatal nutrition emerges as being just as critical for increased developmental ability, with the World Health Organisation (WHO) recommending exclusive breastfeeding as the preferred method of feeding for the first 6 months of life, unless the mother is HIV^+ (Anderson et al., 1999; Grantham-McGregor, et al., 1999; Jain et al., 2002; World Health Organisation (WHO), 2001). Not only does breastfeeding benefit infant development through nutrients in the breast milk, most notably long chain polyunsaturated fatty acids, linked to retinal, neurological and cortical functioning in children, but it has also been shown to reduce infant morbidity as well as develop closer mother-child relations (Grantham–McGregor et al., 1999; Dewey et al., 2001; Daniels & Adair, 2005). Evidence suggests a positive

relationship between breastfeeding and cognitive ability, with breastfed children, on average, scoring higher on general cognitive ability when compared to those formulae fed (Anderson et al., 1999; Grantham-McGregor, et al., 1999; Jain et al., 2002; Jacobson et al., 1999). Further evidence for the link between breastfeeding and cognitive performance comes from a meta-analysis of research showing an average increase in cognitive functioning of around 3 points after adjusting for covariates in children who were breastfed compared to those who were not (Anderson et al., 1999; Beaver et al., 2010; Kramer et al., 2008; Uauy & Peirano, 1999; Uauy & Andraca, 1995). Jacobson et al. (1991) similarly describe preterm children who were breastfed during infancy showed significantly higher IQ scores at 4 and 11 years of age, using the McCarthy Scales of Children's Abilities and Peabody Picture Vocabulary Test-Revised, compared to non-breastfed infants (McGregor et al., 1999; Jacobson et al., 1999; Jain et al., 2002).

Findings from the current study indicate that the longer mothers breastfed their prenatal alcohol exposed infants, the better they performed at 5 years of age over gross motor skills and executive functions. Similarly, the longer children in the Control group were breastfed the better their performance in terms of language abilities during infancy. Previous studies similarly describe positive associations between duration of breastfeeding and developmental ability, with reports from developing countries showing small motor improvements with the longer duration of exclusive breastfeeding. Larger benefits, including those associated with mental development, were reported for babies of low birth weight (Daniels & Adair, 2005; Dewey et al., 2001). Another study conducted on healthy, breastfed children report better performance in terms of language abilities at 10 to 12 years of age (Tozzi et al., 2012).

It remains uncertain as to whether the effect of breastfeeding on cognitive functioning is causal or the result of confounding factors including that of maternal education and maternal IQ. While maternal IQ was not included in the currents study, it is important to consider it and other unexplained variables as explanations for the breastfeeding findings in the present study.

A number of studies have examined the effects of risk factors responsible for the variance of damage in offspring of women reportedly drinking similar amounts of alcohol over similar time points during pregnancy. Findings indicate that older mothers who consume alcohol, with higher rates of gravidity and parity, show greater likelihood of more severely affected children, when compared with women drinking similar patterns and levels (Jacobson et al, 1999; May et al., 2007, 2008; Urban et al., 2008; Viljoen et al., 2002, 2005). While research describes the influence of maternal age, nutritional status, parental intelligence, level of education and general home environment on developmental performance, another important aspect to consider is that of quantity, frequency and timing of the alcohol exposure (Jacobson & Jacobson, 1999; May et al., 2005: Viljoen et al., 2002). Variations in patterns and timing of prenatal alcohol exposure, in combination with the above-mentioned variables, may explain disparities in relationships and identified developmental domains observed in the current study between groups. While certain maternal variables may be related to poor cognitive outcomes for the child, the same maternal variables combined with drinking during pregnancy are likely to result in even poorer consequences.

Although comparisons with previous studies are difficult to make due to differences in sampling, research designs and measurements used, current findings confirm a negative impact of heavy prenatal alcohol exposure and the cumulative effect of socio–economic factors on early childhood development. Furthermore, the findings highlight an important controversy, regarding

whether deficits are derived from prenatal alcohol exposure rather than from the neglectful and/or non-stimulating environment, frequently found amongst heavy drinking mothers or both. What is apparent from the current study is that variables are interrelated. Women from disadvantaged communities, who consume alcohol, place the health and the developmental abilities of their unborn children at risk. By comparing alcohol exposed and non–exposed children from the same resource deprived environment, this study attempted to limit the impact of socio-demographic variables.

Conservative estimates suggest that 200 million children under 5 years of age in developing countries do not reach their full potential (Grantham–McGregor et al., 2007). While the impact of poverty and socio-economic status (SES) on early childhood development is known to be negative, its impact may be substantially higher when prenatal alcohol exposure is also present. When it comes to understanding the full impact that prenatal alcohol exposure has on developmental abilities, behavioural and cognitive dysfunctions during childhood, FAS represents the 'tip of the iceberg'. When examining prenatal alcohol exposure, it is important to consider relevant covariates distinguished by a host of other risk factors (Neuspiel, 1994; Viljoen et al., 2002, 2005). The changing effects associated with prenatal alcohol exposure over time described in the current study are consistent with a range of risk factors including, socio-economic status (SES), ethnic diversity, maternal age, maternal nutrition, timing, and dose of early exposure to alcohol, all of which frequently occur together (Bradley & Corwyn, 2002; Hamadani & Grantham–McGregor, 2004; Baker–Henningham, Powell, Walker & Grantham–McGregor, 2003).

While findings indicate that FAS/PFAS is often the result of a complex interaction between diverse social, political, environmental and genetic risks, they further show that children, regardless of prenatal alcohol exposure, develop in relation to their environment and not in isolation to it (Bronfenbremmer, 1979; Bronfenbrenner & Ceci, 1994). Worryingly, prenatal alcohol exposure seems to be the beginning of an intergenerational pathway to physical, social and later mental ill health issues contributing to the development of a perpetual cycle of adversity. Findings from the current study have important implications for both the early identification of prenatal alcohol exposure and the longitudinal use of the GMDS/ER in research practice.

While most research related to prenatal alcohol exposure has focused on developed countries, the extent of external variables such as, low socio–economic status, maternal nutrition and other factors associated with poverty has necessitated further investigations into the role of prenatal alcohol exposure on early childhood development within these poorly resourced communities. The following section summarises the major findings of the study and their implications, presents the study's limitations while providing recommendations for future research.

5.5 Major findings and implications

In summary, greater developmental deficits were associated with exposure to prenatal alcohol, especially in terms of gross motor and language functioning during infancy. Developmental deficits described in the current study were evident from as early as 7 months of age, which indicates a need for early developmental assessment in at risk populations. At 5 years of age sustained delays were evident in the same prenatal alcohol exposed group over sensorimotor, cognitive and social adaptive functioning domains at 5 years of age. With age, the effects of low

level exposure to prenatal alcohol become more apparent over higher-order cognitive abilities. Overall, results support the evidence that heavy prenatal alcohol exposure influences serious and continued developmental deficits (Bishop et al., 2007; Kodituwakku et al., 2001; McGee et al., 2009; Rasmussen et al., 2009; Roebuck et al., 1998; Schonfield et al., 2006; Valenzuela et al., 2010; Van der Leeden et al., 2001; Whaley et al., 2001). As there is continuing uncertainty regarding the effects of moderate levels of alcohol intake in pregnancy, more research related to this pattern of drinking is required. This study provided a description of the developmental outcomes of children, during their first five years, exposed to varying degrees of alcohol use. Higher-order cognitive abilities were negatively affected by mild to moderate levels of alcohol exposure, without a confirmed FASD diagnosis. The implications of these findings is that there is a need for more accurate documentation of alcohol consumption so that at-risk drinkers are identified earlier (ideally, pre-conception) and offered appropriate interventions to reduce developmental risk to the developing fetus.

Earlier recognition of pregnancy, in the group heavily exposed to alcohol, was associated with better developmental functioning. Arguably, this finding validates the suggestion that early exposure to heavy levels of alcohol in utero, even prior to the confirmation of the pregnancy, produces as adverse effects on fetal brain development as that of exposure throughout the pregnancy (Maier & West, 2001). The prevention of risky drinking during pregnancy could significantly reduce adverse perinatal outcomes with implications for affected families and cost to healthcare systems. As it is likely that FASD is under-recognised, babies born to women who drink alcohol prior to and during pregnancy should be closely monitored in order to, more accurately determine the longitudinal effects of prenatal alcohol exposure in these populations.

These findings highlight the importance of early detection of a pregnancy and of encouraging mothers to change their lifestyles and habits. Pregnant women should continue to be advised that there is no known safe amount of fetal alcohol exposure, and questions about alcohol use prior to recognition of pregnancy should be included in routine clinical and developmental interviews.

Findings from the current study indicate the impact of maternal variables, such as maternal age, marital status, level of education and employment on early childhood development in children with varying degrees of prenatal alcohol exposure. Post natal anthropometric measurements may offer a protective factor, especially amongst those children without a FAS/PFAS diagnosis, but who were exposed to mild-moderate levels of prenatal alcohol. Findings from the current study indicate the links between maternal nutrition and intrauterine environment which play an important role in protecting against later developmental delays associated with mild to moderate levels of prenatal alcohol exposure. These results have practical implications for research. Investigators should consider the impact of socio-economic status differences when designing studies investigating early developmental abilities of children. While the sample size was small, findings from the current study show associations between poverty and poor performance in terms of fine motor ability, language and higher order cognitive abilities. Fewer socio-demographic factors influenced the developmental performance of infants in the FASD group, with maternal education and employment associated with decreased eye hand coordination and language abilities amongst the PAE group. Parity, usually associated with poverty and the lack of stimulation, was found to be associated with poorer language and higher order cognitive abilities amongst the Controls.

Another distinctive finding was the conspicuous lack of significant relationship between subscales of the infant and child versions of the GMDS/ER over time. This suggests that the scales used to assess development between sample groups in infancy may well be measuring different constructs to those at age 5. By implication, this makes it difficult to draw longitudinal conclusions regarding the development of groups using both versions of the GMDS/ER. Global measures of development such as those identified by the GMDS/ER, may not be sensitive enough to detect subtle or specific effects of prenatal alcohol exposure, especially during infancy. Future research should make use of measures that assess specific aspects of infant development, which may be better able to predict later outcomes and prove more useful in detecting the impact of alcohol on brain development. Thus, in light of the paucity of research that has examined the impact of prenatal alcohol exposure the current findings suggest important outcomes relating to the assessment of children with varying degrees of prenatal alcohol exposure, using both versions of the GMDS/ER over time.

5.6 Limitations

While the limitations of the study are typical of longitudinal studies and not unique to the study, a description of them is warranted. Caution is needed when extending these study findings to other populations, as the current study drew on participants from a distinctive, low socio-economic environment where alcohol consumption was high and known FASD rates. Although larger than similar comparative studies, the sample sizes provide limited power to detect differences between groups making it difficult to detect discrepancies amongst developmental abilities during infancy and early childhood. Replication of this study with larger samples and greater access to maternal information, such as maternal IQ levels, BMI and timing of alcohol exposure, would allow for more sophisticated statistical analyses, such as regression analyses.

Unequal group sizes, based on prenatal alcohol exposure, may have further influenced results. Sample attrition and missing data was anticipated in the longitudinal study with, geographical mobility, poor infant and maternal health and general low socio–economic conditions being some of the reasons for the decreased sample. The loss to follow-up in the current study, common in similar high risk, poorly resourced communities, highlights difficulties in retaining such individuals in longitudinal studies (Larrson, Bohlin & Tunnel, 1985). Although group sizes were similar and large enough to explore the psychometric properties of the GMDS/ER, the unknown influence of unequal distribution represents a possible limitation to this study. These limitations were compensated for by the choice of statistical techniques and the collapsing of the study groups for analyses. Another possible explanation for the findings may refer to these statistical analyses used. Since deviations from normality were slight, either parametric or nonparametric analyses were appropriate. Deviations in normality may have been influenced by the presence of legitimate outliers, subsequently retained for analyses. While parametric tests are considered more robust and yield greater statistical power, they prove less sensitive to outliers (Field, 2009). Thus, due to the violations of normality and the inclusion of outliers, nonparametric analyses were used; ensuring that the results could be interpreted with a degree of conviction.

A further limitation relates to the use of the GMDS/ER tool, shown to measure broad abilities in completing a given task, but being unable to allow detailed analyses of more specific delays, especially during infancy (Adnams et al., 2001, Cockcroft et al., 2008). Although both versions of the GMDS/ER have been used extensively in research, direct comparisons between them may be prone to misinterpretation, due to differences in means and standard deviations (Griffiths,

1954; Huntley, 1996; Luiz et al., 2004; Ivens & Martin, 2002). It was hoped that by using converted *z*-scores for both the infants and children data, potential interpretation errors would be overcome. Individually, the psychometric properties of both the Infant Version and the Revised Child version of the GMDS/ER suggest high reliability and good validity, but broader correlational studies are required between versions of the GMDS/ER. Item content during infancy concentrates on motor abilities and social interaction, while at 5 years of age it emphasizes visual perception, spatial relations, memory and executive functions which may account for variations in scores between infant and early childhood assessments and the absence of significant correlations between subscales over time (Luiz et al., 2004). Thus, the findings reported in this study may reflect the outcome measures of versions of the GMDS/ER rather than differences according to age. The current study's findings regarding poor correlations between subscales of the versions of the GMDS/ER may suggest its use as a longitudinal measure of development is less sensitive as it may be tapping differing constructs over time.

Another explanation for the variability in findings across age groups may stem from the general decline in development that occurs over time among children of low socioeconomic status, regardless of prenatal alcohol exposure (Kaplan–Estrin et al., 1999; Laughton et al 2010). Findings from the current study similarly propose that while scores in the first year of life may be over-estimated by the GMDS. With age, subscales become more discerning of developmental delay between alcohol exposed groups, with the exception of the language subscale of the GMDS/ER, which proves less discerning of prenatal alcohol exposure at 5 years of age. While a useful general indicator of developmental delay, the GMDS/ER may not be the most appropriate test when assessing longitudinal developmental delay, especially in children from low socio-economic backgrounds with prenatal alcohol exposure.

Another limitation may lie in the accuracy of the estimates of prenatal alcohol exposure, which prove essential within the context of early childhood development. The retrospective approach to gathering information regarding the method and timing of questions and exact amounts of alcohol consumed by mothers may well represent a loss in accurate information. Furthermore, large variations in alcohol intake make accurate maternal recall difficult, with underreporting likely amongst the PAE group. While reliance on maternal self-reports of alcohol use may have distorted the acquired data due to social desirability in responding, lapse of time or limited ability to recall specific units of alcohol consumed, such self-reports commonly used are considered reliable and valid (Poikolainen, Leppanen & Vuori, 2002; Viljoen et al., 2002). Furthermore, the use of varying units of alcohol and categories associated with maternal drinking make comparing findings between studies difficult. Future research should aim at developing a common set of categories of alcohol use, making findings over all fields of prenatal alcohol exposure, more comparable. It is important to consider the levels of alcohol consumption on the potential impact on developmental ability. Current findings highlight the importance of evaluating the effects of timing and pattern of prenatal alcohol exposure prior to the recognition and throughout the pregnancy, with timing of alcohol exposure directly related to the issue of dosing. Additional data is needed to determine whether drinking earlier versus later during pregnancy has a greater impact on early developmental outcomes. Researchers suggest that continuous heavy drinking throughout pregnancy is associated with lower infant scores using the Brazelton Neonatal Behavioral Assessment Scale , whereas infants whose mothers drink heavily early in pregnancy but who stop do not exhibit the same deficits (Coles et al., 1987). While, important teratogenic consequences have been indicated by the pattern of alcohol consumption, causes of these susceptibilities in the current study were not elucidated, with previous studies attributing

influences to genetic predisposition, nutritional inadequacy and variation in the vulnerability of different brain regions (Abel & Hannigan, 1995; Elliot & Bower, 2004; Maier & West, 2001a,b).

In using the IOM (1996) proposed terminology, many of the children in the current sample would have been diagnosed as having Alcohol Related Neurodevelopmental Disorder (ARND). It is this group which poses the greatest diagnostic challenges and concern to communities, with the absence of FAS/PFAS facial features and presentation of developmental delays. While this study aimed at including a group of children with some prenatal alcohol exposure (PAE) it must be noted that not all children from the PAE group presented with either a small head circumference or evidence of a complex pattern of behavioural or cognitive abnormalities, diagnostic criteria required for an ARND diagnosis, as described in section 2.3. Future developmental studies directed towards to the impact of mild to moderate levels of prenatal alcohol exposure, without classic FASD features.

Finally, confident comparisons between the current study and other research are complicated by different measurements of assessment used, varied sample sizes, age of participants, alcohol exposure levels and differences in methodologies used (Mattson et al., 2011).
Despite these limitations, certain tentative conclusions can be drawn from the present study with regard to the impact of socio-environmental factors, present in the community, which appear to contribute to the nature and extend of developmental delay, regardless of prenatal alcohol exposure.

5.7 Conclusions

In light of the above findings, implications and limitations, the present study has confirmed evidence that heavy prenatal alcohol exposure is detrimental to early gross motor and language abilities with evidence of later deficits associated with higher-order cognitive abilities. With age, children exposed to moderate levels of prenatal alcohol exposure, but with no physical features of FASD, present with higher-order cognitive delays, confounding the detection of early developmental deficits. This study emphasises the need for improved, timely detection and management of alcohol exposure during early pregnancy, often even prior to the recognition of the pregnancy, influencing the effectiveness of early intervention in minimising later developmental deficits. The study contributes important information regarding the longitudinal associations between developmental constructs measured between versions of the GMDS/ER. While each version provides a reliable and valid indication of childhood development, longitudinal correlations between versions prove less accurate and warrant further investigation, in both well-resourced and under resourced communities.

Reference List

Abel, E. L. (1995). An update on incidence of FAS: FAS is not an equal opportunity birth defect. *Neurotoxicology and Teratology, 17*(4), 437-443.

Abel, E. L., & Hannigan, J. H. (1995). Maternal risk factors in fetal alcohol syndrome: Provocative and permissive influences. *Neurotoxicology and Teratology, 17*(4), 445-462.

Abel, E. L., Kruger, M. L., & Friedl, J. (1998). How do physicians define "light," "moderate," and "heavy" drinking? *Alcoholism, Clinical and Experimental Research, 22*(5), 979-984.

Abel, E. L. (2001). The gin epidemic: much ado about what? *Alcohol Alcohol, 36*(5), 401-405.

Abkarian, G. G. (1992). Communication effects of prenatal alcohol exposure. *Journal of Communication Disorders, 25*(4), 221-240.

Addison, J.T. (1992). Urie Bronfenbrenner. *Human Ecology*, *20* (2), 16-20.

Adnams, C. M., Kodituwakku, P. W., Hay, A., Molteno, C. D., Viljoen, D., & May, P. A. (2001). Patterns of cognitive-motor development in children with fetal alcohol syndrome from a community in south africa. *Alcoholism, Clinical and Experimental Research, 25*(4), 557-562.

Allan, M. M. (1988). *A comparison of the performance of normal preschool South African and British children on the Griffiths Scales of Mental Development*. (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Allan, M. M. (1992). *The performance of South African normal preschool children on the Griffiths Scales of Mental Development: A comparative study.* (Unpublished doctoral thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Anderson, V. (1998). Assessing executive functions in children: Biological, psychological, and developmental considerations. *Neuropsychological Rehabilitation, 8*(3), 319-349.

Anderson, J. W., Johnstone, B. M., & Remley, D. T. (1999). Breast-feeding and cognitive development: A meta-analysis. *The American Journal of Clinical Nutrition, 70*(4), 525-535.

Aragon, A. S., Kalberg, W. O., Buckley, D., Barela-Scott, L. M., Tabachnick, B. G., & May, P. A. (2008). Neuropsychological study of FASD in a sample of american indian children: Processing simple versus complex information. *Alcoholism, Clinical and Experimental Research, 32*(12), 2136-2148.

Arceneaux, J.M., Cheramie, G.M., & Smith, C.W. (1996). Gender differences in WAIS-R age-corrected scaled scores. *Perceptual and Motor Skills, 83,* 1211-1215.

Archibald, S. L., Fennema-Notestine, C., Gamst, A., Riley, E. P., Mattson, S. N., & Jernigan, T. L. (2001). Brain dysmorphology in individuals with severe prenatal alcohol exposure. *Developmental Medicine & Child Neurology, 43*(03), 148.

Arvedson, P. J. (2002). Young children with specific language impairment and their numerical cognition. *Journal of Speech, Language, and Hearing Research : JSLHR, 45*(5), 970-982.

Astley, S. J., & Clarren, S. K. (2000). Diagnosing the full spectrum of fetal alcohol-exposed individuals: Introducing the 4-digit diagnostic code. *Alcohol and Alcoholism , 35*(4), 400-410.

Athey, C. (1990). *Extending thought in young children: A parent-teacher partnership*. London: Paul Chapman.

Autti-Ramo, I., & Granstrom, M. L. (1991). The effect of intrauterine alcohol exposition in various durations on early cognitive development. *Neuropediatrics, 22*(4), 203-210.

Baker-Henningham, H., Powell, C., Walker, S., & Grantham-McGregor, S. (2003). Mothers of undernourished jamaican children have poorer psychosocial functioning and this is associated with stimulation provided in the home. *European Journal of Clinical Nutrition, 57*(6), 786-792.

Barbarin, O. A., & Richter, L. (2001). Economic status, community danger and psychological problems among south african children. *Childhood , 8*(1), 115-133.

Barbarin, O.A., & N. Khomo. (1997) `Indicators of Economic Status and Social Capital in South African Townships: What Do They Reveal about the Material And Social Conditions In Families Of Poor Children? Childhood, *4*(2), 193-222.

Barnard, A. (2000). *The Griffiths' Practical Reasoning Scale: A Revision.* (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Barnard, A. (2003). Exploring the validity of the Revised Griffiths' Practical-Reasoning Subscale in the British Isles. (Unpublished doctoral thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Barr, H.M., Streissguth, A.P., Darby, B.L., & Sampson, P.D. (1990). *Prenatal exposure to alcohol, tobacco, aspirin, effects on fine and gross motor performance in 4–year old children*. Dev Psychol, *26*, 339 – 348.

Beail, N. (1985). A comparative study of profoundly multiply handicapped children's scores on the bayley and the griffiths developmental scales. *Child: Care, Health and Development, 11*(1), 31-36.

Beattie, J. O., Day, R. E., Cockburn, F., & Garg, R. A. (1983). Alcohol and the fetus in the west of scotland. *British Medical Journal (Clinical Research Ed.), 287*(6384), 17-20.

Beaver, K. M., Vaughn, M. G., DeLisi, M., & Higgins, G. E. (2010). The biosocial correlates of neuropsychological deficits: Results from the national longitudinal study of adolescent health. *International Journal of Offender Therapy and Comparative Criminology, 54*(6), 878-894.

Becker, M., Warr-Leeper, G. A., & Leeper, H. A.,Jr. (1990). Fetal alcohol syndrome: A description of oral motor, articulatory, short-term memory, grammatical, and semantic abilities. *Journal of Communication Disorders, 23*(2), 97-124.

Berglund, E., Eriksson, M., & Westerlund, M. (2005). Communicative skills in relation to gender, birth order, child care and socio-economic status in 18-month-old children. *Scandinavian Journal of Psychology, 46,* 485-491.

Bertrand, J., Floyd, L. L., Weber, M. K., & Fetal Alcohol Syndrome Prevention Team, Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC). (2005).

Guidelines for identifying and referring persons with fetal alcohol syndrome. *MMWR.Recommendations and Reports : Morbidity and Mortality Weekly Report.Recommendations and Reports / Centers for Disease Control, 54*(RR-11), 1-14.

Benner, S.M. (1992). *Assessing young children with special needs.* White Plains, New York: Longman.

Bhamjee, R.A. (1991). *A comparison of the performance of normal British and South African children on the Griffiths Mental Developmental Scales*. (Unpublished doctoral thesis). University of Port Elizabeth, Port Elizabeth. South Africa.

Bhutta, A. T., Cleves, M. A., Casey, P. H., Cradock, M. M., & Anand, K. J. (2002). Cognitive and behavioral outcomes of school-aged children who were born preterm: A meta-analysis. *JAMA : The Journal of the American Medical Association, 288*(6), 728-737.

Bidder, R. T., Bryant, G., & Gray, O. P. (1975). Benefits to down's syndrome children through training their mothers. *Archives of Disease in Childhood, 50*(5), 383-386.

Bishop, S., Gahagan, S., & Lord, C. (2007). Re-examining the core features of autism: A comparison of autism spectrum disorder and fetal alcohol spectrum disorder. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 48*(11), 1111-1121.

Bjorklund, D. F., & Bjorklund, B. R. (1992). Looking at children: An introduction to child development. Pacific Grove, California: Brooks/Cole Publishing Company.

Blakemore, J.E.O., Berenbaum, S.A., & Liben, L.S. (2009). *Gender development*. New York: Taylor & Francis Group, LLC.

Bloom, L. (1998). Language acquisition and its developmental context. In D. Kuhn & R. S. Siegler (Eds.), *Handbook of Child Psychology, 5th edition. Volume 2: Cognition, Perception and Language.* (pp. 1-50). New York: John Wiley.

Bloomfield, K., Stockwell, T., Gmel, G., & Rehn, N. (2003). International comparisons of alcohol consumption. *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism, 27*(1), 95-109.

Bondurant-Utz, J. A., & Luciano, L. B. (1994*). A practical guide to infant and preschool assessment in special education.* Boston: Allyn and Bacon.

Bookstein, F. L., Sampson, P. D., Streissguth, A. P., & Connor, P. D. (2001). Geometric morphometrics of corpus callosum and subcortical structures in the fetal-alcohol-affected brain. *Teratology, 64*(1), 4-32.

Born, M.P., Bleichrodt, N., & Van der Flier, H. (1987). Cross-cultural comparison of sex-related differences on intelligence tests: A meta-analysis. *Journal of Cross-Cultural Psychology, 18,* 283-314.

Bove, I., Miranda, T., Campoy, C., Uauy, R., & Napol, M. (2012). Stunting, overweight and child development impairment go hand in hand as key problems of early infancy: Uruguayan case. *Early Human Development, 88*(9), 747-751.

Bowlby, J. (2000). *Attachment*. New York: Basic Books.

Bradley, R. H., & Corwyn, R. F. (2002). Socioeconomic status and child development. *Annual Review of Psychology, 53*, 371-399.

Brennan, T. L., Funk, S. G., & Frothingham, T. E. (1985). Disproportionate intra-uterine head growth and developmental outcome. *Developmental Medicine and Child Neurology, 27*(6), 746-750.

Breitmayer, B. J., & Ramey, C. T. (1986). Biological nonoptimality and quality of postnatal environment as codeterminants of intellectual development. *Child Development, 57*(5), 1151-1165.

Breakwall, G.M., Hammond, S., Fife-Shaw, C., & Smith, J.A. (2006). *Research methods in psychology* (3rd ed.). London: Sage Publications Ltd.

Brooks-Gunn, J., & Duncan, G. J. (1997). The effects of poverty on children. *The Future of Children / Center for the Future of Children, the David and Lucile Packard Foundation, 7*(2), 55-71.

Brooks-Gunn, J., Guo, G., & Furstenberg, F. (1993). Who drops out of and who continues beyond high school? *Journal of Research on Adolescence*, *3*, 271-294.

Brooks-Gunn, J., Klebanov, P. K., & Duncan, G. J. (1996). Ethnic differences in children's intelligence test scores: Role of economic deprivation, home environment, and maternal characteristics. *Child Development, 67*(2), 396-408.

Bronfenbremmer, U. (1979). *The Ecology of Human Development: Experiments by Nature and Design.* Harvard University Press.

Bronfenbrenner, U., & Ceci, S. J. (1994). Nature-nurture reconceptualised in developmental perspective: A bioecological model. *Psychological Review*, 101, 568-586.

Brown, J. L., & Pollitt, E. (1996). Malnutrition, poverty and intellectual development. *Scientific American, 274*(2), 38-43.

Burd, L., Klug, M. G., Martsolf, J. T., & Kerbeshian, J. (2003). Fetal alcohol syndrome: Neuropsychiatric phenomics. *Neurotoxicology and Teratology, 25*(6), 697-705.

Burden, M. J., Jacobson, S. W., & Jacobson, J. L. (2005). Relation of prenatal alcohol exposure to cognitive processing speed and efficiency in childhood. *Alcoholism: Clinical and Experimental Research, 29*(8), 1473-1483.

Burden, M. J., Jacobson, S. W., Sokol, R. J., & Jacobson, J. L. (2005). Effects of prenatal alcohol exposure on attention and working memory at 7.5 years of age. *Alcoholism: Clinical and Experimental Research, 29*(3), 443-452.

Bushnell, E. W., & Boudreau, J. P. (1993). Motor development and the mind: The potential role of motor abilities as a determinant of aspects of perceptual development. *Child Development, 64*(4), 1005-1021.

Bygren, L. O., Kaati, G., & Edvinsson, S. (2001). Longevity determined by paternal ancestors' nutrition during their slow growth period. *Acta Biotheoretica, 49*(1), 53-59.

Caley, L. M., Kramer, C., & Robinson, L. K. (2005). Fetal alcohol spectrum disorder. *The Journal of School Nursing : The Official Publication of the National Association of School Nurses, 21*(3), 139-146.

Carmichael-Olsen, H., Ohlemiller, M., O'Connor, M., Brown, C., Morris, C. & Damus, K. (2009). *A call to action. Advancing essential services and research on Fetal Alcohol Spectrum Disorders.* A report of the National Task Force on Fetal Alcohol Syndrome and

Fetal Alcohol Effects. National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect Post Exposure Writing Group.

Carmichael Olson, H., Streissguth, A.P., Sampson, P.D., Barr, H.M., Bookstein, F.L., & Thiede, K. (1997). Association of prenatal alcohol exposure with behavioural and learning problems in early adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(9), 1187-1194.

Carney, L. J., & Chermak, G. D. (1991). Performance of american indian children with fetal alcohol syndrome on the test of language development. *Journal of Communication Disorders, 24*(2), 123-134.

Carr, J. L., Agnihotri, S., & Keightley, M. (2010). Sensory processing and adaptive behavior deficits of children across the fetal alcohol spectrum disorder continuum. *Alcoholism, Clinical and Experimental Research, 34*(6).

Chandler, L. S., Richardson, G. A., Gallagher, J. D., & Day, N. L. (1996). Prenatal exposure to alcohol and marijuana: Effects on motor development of preschool children. *Alcoholism, Clinical and Experimental Research, 20*(3), 455-461.

Chetty, C.M. (2012). Fetal Alcohol Spectrum Disorder (FASD) from Infancy to Childhood: Neuropsychological Development and Maternal Depression. (Unpublished doctoral thesis). University of Witwatersrand, Johannesburg, South Africa.

Chersich, M. F., Urban, M., Olivier, L., Davies, L. A., Chetty, C., & Viljoen, D. (2012). Universal prevention is associated with lower prevalence of fetal alcohol spectrum

disorders in northern cape, south africa: A multicentre before-after study. *Alcohol and Alcoholism , 47*(1), 67-74.

Chomsky, N. (1959). A Review of B.F.Skinner's verbal behaviour. *Language*, 35, (1) (1959), 26-58.

Chudley, A. E., Conry, J., Cook, J. L., Loock, C., Rosales, T., LeBlanc, N., & Public Health Agency of Canada's National Advisory Committee on Fetal Alcohol Spectrum Disorder. (2005). Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *CMAJ : Canadian Medical Association Journal, 172*(5 Suppl), S1-S21.

Chudley, A. E., Kilgour, A. R., Cranston, M., & Edwards, M. (2007). Challenges of diagnosis in fetal alcohol syndrome and fetal alcohol spectrum disorder in the adult. *American Journal of Medical Genetics.Part C, Seminars in Medical Genetics, 145C*(3), 261-272.

Church, M. W., Eldis, F., Blakley, B. W., & Bawle, E. V. (1997). Hearing, language, speech, vestibular, and dentofacial disorders in fetal alcohol syndrome. *Alcoholism, Clinical and Experimental Research, 21*(2), 227-237.

Cicero, T.J. (1994). Effects of paternal exposure to alcohol on offspring development. *Alcohol Health & Research World*; *18*(1), 37-41.

Clarke, M. E., & Gibbard, W. B. (2003). Overview of fetal alcohol spectrum disorders for mental health professionals. *The Canadian Child and Adolescent Psychiatry Review, 12*(3), 57-63.

Clarren, S. K., Alvord, E. C.,Jr, Sumi, S. M., Streissguth, A. P., & Smith, D. W. (1978). Brain malformations related to prenatal exposure to ethanol. *The Journal of Pediatrics, 92*(1), 64-67.

Cockcroft, K., Amod, Z., & Soellaart, B. (2008). Level of maternal education and performance of black, south african infants on the 1996 griffiths mental development scales. *African Journal of Psychiatry, 11*(1), 44-50.

Coggins, T. E., Timler, G. R., & Olswang, L. B. (2007). A state of double jeopardy: Impact of prenatal alcohol exposure and adverse environments on the social communicative abilities of school-age children with fetal alcohol spectrum disorder. *Language, Speech, and Hearing Services in Schools, 38*(2), 117-127.

Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). New York: Academic.

Cohen, I. L. (2003). Criterion-related validity of the PDD behavior inventory. *Journal of Autism and Developmental Disorders, 33*(1), 47-53.

Coles, C.D. (1995). Children of parents who abuse drugs and alcohol. In : G.H. Smith, C.D. Coles, M.K. Poulsen & C.K. Cole (Eds.), *Children, Families, and Substance Abuse* (pp. 3-23). USA: Paul H Brookes Publishing Co.

Coles, C. D., Brown, R. T., Smith, I. E., Platzman, K. A., Erickson, S., & Falek, A. (1991). Effects of prenatal alcohol exposure at school age. I. physical and cognitive development. *Neurotoxicology and Teratology, 13*(4), 357-367.

Coles, C. D., Lynch, M. E., Kable, J. A., Johnson, K. C., & Goldstein, F. C. (2010). Verbal and nonverbal memory in adults prenatally exposed to alcohol. *Alcoholism, Clinical and Experimental Research, 34*(5), 897-906.

Coles, C.D., Platzman, K.A., Raskind-Hood, C.L., Brown, R.T., Falek, A., & Smith, I.E. (1997). A comparison of children affected by prenatal alcohol exposure and attention deficit, hyperactivity disorder. *Alcohol Clin Exp Res*, *21*(1), 150-161.

Coles, C. D., Platzman, K. A., Smith, I., James, M. E., & Falek, A. (1992). Effects of cocaine and alcohol use in pregnancy on neonatal growth and neurobehavioral status. *Neurotoxicology and Teratology, 14*(1), 23-33.

Coles, C. D., Smith, I. E. and Falek, A. (1987) Prenatal alcohol exposure and infant behavior: Immediate effects and implications for later development. Advances in Alcohol and Substance Abuse *6*, 87–104.

Connor, P. D., Sampson, P. D., Bookstein, F. L., Barr, H. M., & Streissguth, A. P. (2000). Direct and indirect effects of prenatal alcohol damage on executive function. *Developmental Neuropsychology, 18*(3), 331-354.

Connor, P. D., Sampson, P. D., Streissguth, A. P., Bookstein, F. L., & Barr, H. M. (2006). Effects of prenatal alcohol exposure on fine motor coordination and balance: A study of two adult samples. *Neuropsychologia, 44*(5), 744-751.

Conry, J. (1990). Neuropsychological deficits in fetal alcohol syndrome and fetal alcohol effects. *Alcoholism, Clinical and Experimental Research, 14*(5), 650-655.

Coplan, J., Contello, K. A., Cunningham, C. K., Weiner, L. B., Dye, T. D., Roberge, L., . . . Kirkwood, K. (1998). Early language development in children exposed to or infected with human immunodeficiency virus. *Pediatrics, 102*(1), e8.

Cortese, B. M., Moore, G. J., Bailey, B. A., Jacobson, S. W., Delaney-Black, V., & Hannigan, J. H. (2006). Magnetic resonance and spectroscopic imaging in prenatal alcohol-exposed children: Preliminary findings in the caudate nucleus. *Neurotoxicology and Teratology, 28*(5), 597-606.

Crocker, N., Vaurio, L., Riley, E. P., & Mattson, S. N. (2009). Comparison of adaptive behavior in children with heavy prenatal alcohol exposure or attention-deficit/hyperactivity disorder. *Alcoholism, Clinical and Experimental Research, 33*(11), 2015-2023.

Daniels, M. C., & Adair, L. S. (2005). Breast-feeding influences cognitive development in filipino children. *The Journal of Nutrition, 135*(11), 2589-2595.

Davies, L., Dunn, M., Chersich, M., Urban, M., Chetty, C., Olivier, L., & Viljoen, D. (2011). Developmental delay of infants and young children with and without fetal alcohol spectrum disorder in the northern cape province, south africa. *African Journal of Psychiatry, 14*(4), 298-305.

Dewey, K. G., Cohen, R. J., Brown, K. H., & Rivera, L. L. (2001). Effects of exclusive breastfeeding for four versus six months on maternal nutritional status and infant motor development: Results of two randomized trials in honduras. *The Journal of Nutrition, 131*(2), 262-267.

Ebrahim, S. H., Luman, E. T., Floyd, R. L., Murphy, C. C., Bennett, E. M., & Boyle, C. A. (1998). Alcohol consumption by pregnant women in the united states during 1988-1995. *Obstetrics and Gynecology, 92*(2), 187-192.

Edwards, O.L. (1975). Cohort and sex changes in black educational achievement. *Sociology and Social Research*, *59(2*), 110-120.

Elliott, E. J., & Bower, C. (2004). FAS in australia: Fact or fiction? *Journal of Paediatrics and Child Health, 40*(1-2), 8-10.

Engle, P. L., Black, M. M., Behrman, J. R., Cabral de Mello, M., Gertler, P. J., Kapiriri, L., . . . International Child Development Steering Group. (2007). Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. *Lancet, 369*(9557), 229-242.

Ensminger, M.E., & Fothergill, K.E. (2003). A decade of measuring SES: what it tells us and where to go from here. In M.H. Bornstein & R.H. Bradley (Eds), *Socioeconomic status, parenting and child development* (pp.13-27). Mahwah: Lawrence Erlbaum.

Erikson, E. H. (1982). *The life cycle completed.* New York:Norton

Ernhart, C. B., Wolf, A. W., Linn, P. L., Sokol, R. J., Kennard, M. J., & Filipovich, H. F. (1985). Alcohol-related birth defects: Syndromal anomalies, intrauterine growth retardation, and neonatal behavioral assessment. *Alcoholism, Clinical and Experimental Research, 9*(5), 447-453.

Falgreen Eriksen, H. L., Mortensen, E. L., Kilburn, T., Underbjerg, M., Bertrand, J., Stovring, H., . . . Kesmodel, U. S. (2012). The effects of low to moderate prenatal alcohol exposure

in early pregnancy on IQ in 5-year-old children. *BJOG : An International Journal of Obstetrics and Gynaecology, 119*(10), 1191-1200.

Fattal-Valevski, A., Leitner, Y., Kutai, M., Tal-Posener, E., Tomer, A., Lieberman, D., . . . Harel, S. (1999). Neurodevelopmental outcome in children with intrauterine growth retardation: A 3-year follow-up. *Journal of Child Neurology, 14*(11), 724-727.

Fenson, L., Dale, P.S., Reznick, J.S, Bates, E., Thal, D.J., & Pethick, S.J. (1994). Variability in early communicative development. *Monographs of the Society for Research in Child Development, 59*(5, Serial No. 242).

Field, A. (2009). *Discovering Statistic Using SPSS*. (3rd ed): Sage Publications Ltd

Floyd, R. L., Decoufle, P., & Hungerford, D. W. (1999). Alcohol use prior to pregnancy recognition. *American Journal of Preventive Medicine, 17*(2), 101-107.

Floyd, R. L., Ebrahim, S. H., Boyle, C. A., & Gould, D. W. (1999). Observations from the CDC. preventing alcohol-exposed pregnancies among women of childbearing age: The necessity of a preconceptional approach. *Journal of Women's Health & Gender-Based Medicine, 8*(6), 733-736.

Flynn, H. A., & Chermack, S. T. (2008). Prenatal alcohol use: The role of lifetime problems with alcohol, drugs, depression, and violence. *Journal of Studies on Alcohol and Drugs, 69*(4), 500-509.

Foster, R.K., & Marriott, H.E. (2006). Alcohol consumption in the new millennium- weighing up the risks and benefits for our health. *Nutrition Bulletin*, *31*, 286-331.

Fried, P. A., O'Connell, C. M., & Watkinson, B. (1992). 60- and 72-month follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol: Cognitive and language assessment. *Journal of Developmental and Behavioral Pediatrics : JDBP, 13*(6), 383-391.

Fried, P. A., & Watkinson, B. (1988). 12- and 24-month neurobehavioural follow-up of children prenatally exposed to marihuana, cigarettes and alcohol. *Neurotoxicology and Teratology, 10*(4), 305-313.

Fried, P. A., & Watkinson, B. (1990). 36- and 48-month neurobehavioral follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol. *Journal of Developmental and Behavioral Pediatrics : JDBP, 11*(2), 49-58.

Gale, C. R., O'Callaghan, F. J., Bredow, M., Martyn, C. N., & Avon Longitudinal Study of Parents and Children Study Team. (2006). The influence of head growth in fetal life, infancy, and childhood on intelligence at the ages of 4 and 8 years. *Pediatrics, 118*(4), 1486-1492.

Gallahue, D.L., & Ozmann, J.C. (1995). *Understanding motor development: Infants, children, adolescents, adults* (3rd ed.). Madison, WI: Brown & Benchmark.

Galsworthy, M.J., Dionne, G., Dale, P.S., & Plomin, R. (2000). Sex differences in early verbal and non-verbal cognitive development. *Developmental Science, 3,* 206-215.

Garcia-Alix, A., Saenz-de Pipaon, M., Martinez, M., Salas-Hernandez, S., & Quero, J. (2004). Ability of neonatal head circumference to predict long-term neurodevelopmental outcome. *Revista De Neurologia, 39*(6), 548-554.

George, M.D. (1966). *London Life in the XVIIIth Century*: Alfred A. Knopf, New York

Giagazoglou, P., Kyparos, A., Fotiadou, E., & Angelopoulo, N. (2007). The effect of residence area and mothers education on motor development of preschool-aged children in Greece. *Early Child Development and Care*, *177*(5), 479-492.

Glascoe, F. P. (2001). Are overreferrals on developmental screening tests really a problem? *Archives of Pediatrics & Adolescent Medicine, 155*(1), 54-59.

Goldschmidt, L., Richardson, G. A., Stoffer, D. S., Geva, D., & Day, N. L. (1996). Prenatal alcohol exposure and academic achievement at age six: A nonlinear fit. *Alcoholism, Clinical and Experimental Research, 20*(4), 763-770.

Goodlett, C. R., Gilliam, D. M., Nichols, J. M., & West, J. R. (1989). Genetic influences on brain growth restriction induced by development exposure to alcohol. *Neurotoxicology, 10*(3), 321-334.

Goodlett, C. R., & Horn, K. H. (2001). Mechanisms of alcohol-induced damage to the developing nervous system. *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism, 25*(3), 175-184.

Gottlieb, G. (1991). Experiential canalization of behavioral development: theory. *Developmental Psychology, 27*(1), 4-13.

Grantham-McGregor, S., Cheung, Y. B., Cueto, S., Glewwe, P., Richter, L., Strupp, B., & International Child Development Steering Group. (2007). Developmental potential in the first 5 years for children in developing countries. *Lancet, 369*(9555), 60-70.

Grantham-McGregor, S. M., & Fernald, L. C. (1997). Nutritional deficiencies and subsequent effects on mental and behavioral development in children. *The Southeast Asian Journal of Tropical Medicine and Public Health, 28 Suppl 2*, 50-68.

Grantham-McGregor, S., Fernald, I., & Sethuraman, K. (1999). Effects of health and nutrition on cognitive and behavioral development in the first 3 years of life. Part 2. Infections and micronutrient deficiencies: iodine, iron and zinc. *Food Nutr Bull*, *20*, 76-99.

Green, J. H. (2007). Fetal alcohol spectrum disorders: Understanding the effects of prenatal alcohol exposure and supporting students. *The Journal of School Health, 77*(3), 103-108.

Greenbaum, R., Nulman, I., Rovet, J., & Koren, G. (2002). The toronto experience in diagnosing alcohol-related neurodevelopmental disorder: A unique profile of deficits and assets. *The Canadian Journal of Clinical Pharmacology, 9*(4), 215-225.

Greene, T., Ernhart, C. B., Ager, J., Sokol, R., Martier, S., & Boyd, T. (1991). Prenatal alcohol exposure and cognitive development in the preschool years. *Neurotoxicology and Teratology, 13*(1), 57-68.

Greene, T., Ernhart, C. B., Martier, S., Sokol, R., & Ager, J. (1990). Prenatal alcohol exposure and language development. *Alcoholism, Clinical and Experimental Research, 14*(6), 937-945.

Greenop, K. T. (2004). *The development of literacy skills in Zulu and Northern Sotho speaking children : a cognitive-neuropsychological investigation (Unpublished doctoral dissertation).* University of the Witwatersrand, Johannesburg, South Africa.

Griffiths, R. (1954). *The abilities of babies*. London: Child Development Research Centre.

Griffiths, R. (1970). *The abilities of young children*. London: Child Development Research Centre.

Griffiths, R. (1986). *The abilities of babies*. Amersham: Association for Research in Infant and Child Development (ARICD).

Guerri, C., Bazinet, A., & Riley, E. P. (2009). Foetal alcohol spectrum disorders and alterations in brain and behaviour. *Alcohol and Alcoholism (Oxford, Oxfordshire), 44*(2), 108-114.

Gusella, J. L., & Fried, P. A. (1984). Effects of maternal social drinking and smoking on offspring at 13 months. *Neurobehavioral Toxicology and Teratology, 6*(1), 13-17.

Hack, M., Klein, N. K., & Taylor, H. G. (1995). Long-term developmental outcomes of low birth weight infants. *The Future of Children / Center for the Future of Children, the David and Lucile Packard Foundation, 5*(1), 176-196.

Hall, L. C. (1971a). Balvicar Centre after five years (Survey of a child development centre for preschool handicapped children). *Community Medicine*, *126* (3288), 93-98.

Hall, L. C. (1971b). Balvicar Centre after five years (Survey of a child development centre for preschool handicapped children). *Community Medicine*, *126*(3289), 105-109.

Halliday, H. L., Reid, M. M., & McClure, G. (1982). Results of heavy drinking in pregnancy. *British Journal of Obstetrics and Gynaecology, 89*(11), 892-895.

Halpern, D.F. (1993). Sex, brains and hands: Gender differences in cognitive abilities. *Skeptic, 2(3)*, 96-103.

Halpern, D.F. (1997). Sex differences in intelligence: Implications for education. *American Psychologist, 52,* 1091-1102.

Halpern, D.F. (2000). *Sex differences in cognitive abilities* (3rd ed.). Mahwah, NJ: Lawrence Erlbaum Associates.

Hamadani, J., & Grantham-McGregor, S. M. (2004). Report of the family care indicators project: Validating the family psychosocial indicators in rural Bangladesh. Report to UNICEF Early Child Development Desk. Retrieved from http://www.biomedcentral.com/1471-2458/12/622

Hanlon, H.W., Thatcher, R.W., & Cline, J. (1999). Gender differences in the deveolopment of EEG coherence in normal children. *Development Neuropsychology*, 16 (3), 479-506.

Hannigan, J. H., & Berman, R. F. (2000). Amelioration of fetal alcohol-related neurodevelopmental disorders in rats: Exploring pharmacological and environmental treatments. *Neurotoxicology and Teratology, 22*(1), 103-111.

Hannigan, J. H., Berman, R. F., & Zajac, C. S. (1993). Environmental enrichment and the behavioral effects of prenatal exposure to alcohol in rats. *Neurotoxicology and Teratology, 15*(4), 261-266.

Hanson, R. (1982). Item reliability for the griffiths scales of mental development. *Child: Care, Health and Development, 8*(3), 151-161.

Harrison. B. (1967). Drink and Sobriety in England 1815–1872. *International Review of Social History*, *12*, 204-276.

Hart, B., & Risley, T. R. (1995). *Meaningful differences in the everyday experience of young American children*. Baltimore, MD: Paul Brookes.

Heimes, L. (1983). *The comparison of the JSAIS and the Griffiths Developmental Scale scores of 3-5 year old boys and girls. (*Unpublished master's thesis).University of Port Elizabeth, Port Elizabeth, South Africa.

Hegedus, A. M., Alterman, A. I., & Tarter, R. E. (1984). Learning achievement in sons of alcoholics. *Alcoholism, Clinical and Experimental Research, 8*(3), 330-333.

Henderson, J., Gray, R., & Brocklehurst, P. (2007). Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *BJOG : An International Journal of Obstetrics and Gynaecology, 114*(3), 243-252.

Herbert, J. S., Eckerman, C. O., & Stanton, M. E. (2003). The ontogeny of human learning in delay, long-delay, and trace eyeblink conditioning. *Behavioral Neuroscience, 117*(6), 1196-1210.

Herman, L. E., Acosta, M. C., & Chang, P. N. (2008). Gender and attention deficits in children diagnosed with a fetal alcohol spectrum disorder. *The Canadian Journal of Clinical Pharmacology, 15*(3), e411-9.

Hooper, S. R., Burchinal, M., Roberts, J. E., Zeisel, S., & Neebe, E. C. (1998). Social and family risk factors for infant development at one year: An application of the cumulative risk model. *Journal of Applied Developmental Psychology, 19*(1), 85-96.

Hong, M., & Krauss, R. S. (2012). Cdon mutation and fetal ethanol exposure synergize to produce midline signaling defects and holoprosencephaly spectrum disorders in mice. *PLoS Genetics, 8*(10), e1002999.

Houston-McMillan, J. E. (1988). Borderline mental handicapped preschoolers: Identification and treatment evaluation using the Griffiths Scales of Mental Development. In D. M. Luiz (Ed.), *Griffiths Scales of Mental Development: South African studies* (Research Papers No. C25) (pp. 52-58). Port Elizabeth, South Africa: University of Port Elizabeth.

Howell, D.C. (2002). Statistical methods for psychology (5th ed). Australia: Thomson Learning Inc.

Howell, K. K., Lynch, M. E., Platzman, K. A., Smith, G. H., & Coles, C. D. (2006). Prenatal alcohol exposure and ability, academic achievement, and school functioning in adolescence: A longitudinal follow-up. *Journal of Pediatric Psychology, 31*(1), 116-126.

Hoyme, H. E., May, P. A., Kalberg, W. O., Kodituwakku, P., Gossage, J. P., Trujillo, P. M., . . . Robinson, L. K. (2005). A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: Clarification of the 1996 institute of medicine criteria. *Pediatrics, 115*(1), 39-47.

Humphriss, R., Hall, A., & Macleod, J. (2010). Prenatal alcohol exposure and childhood balance: A systematic review. *Paediatric and Perinatal Epidemiology, 24*(2), 156-165.

Hunt, P. S., Jacobson, S. E., & Torok, E. J. (2009). Deficits in trace fear conditioning in a rat model of fetal alcohol exposure: Dose-response and timing effects. *Alcohol (Fayetteville, N.Y.), 43*(6), 465-474.

Huntley, M. (1996). *The Griffiths Mental Development. From birth to 2 years. Manual.* (Revision). United Kingdom: Association for Research in Infant and Child Development (ARICD).

Hyde, J.S., & McKinley, N.M. (1997). Gender differences in cognition: Results from meta-analyses. In P.J. Caplan, M. Crawford, J.S. Hyde & J.T.E. Richardson (Eds.). *Gender differences in human cognition* (pp. 30-51). New York: Oxford University Press.

Hussong, A. M., Huang, W., Curran, P. J., Chassin, L., & Zucker, R. A. (2010). Parent alcoholism impacts the severity and timing of children's externalizing symptoms. *Journal of Abnormal Child Psychology, 38*(3), 367-380.

Institute of Medicine. (1996). Fetal alcohol syndrome: diagnosis, epidemiology, prevention, intervention, research. Washington, DC: National Academy Press.

Ivens, J., & Martin, N. (2002). A common metric for the griffiths scales. *Archives of Disease in Childhood, 87*(2), 109-110.

Jackson, W. (1995). *Methods: Doing Social Research.* Canada: Prentice-Hall

Jacobson, J. L., & Jacobson, S. W. (1999). Drinking moderately and pregnancy. effects on child development. *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism, 23*(1), 25-30.

Jacobson, J. L., Jacobson, S. W., Sokol, R. J., Martier, S. S., Ager, J. W., & Kaplan-Estrin, M. G. (1993). Teratogenic effects of alcohol on infant development. *Alcoholism, Clinical and Experimental Research, 17*(1), 174-183.

Jacobson, S. W., Jacobson, J. L., & Sokol, R. J. (1994). Effects of fetal alcohol exposure on infant reaction time. *Alcoholism, Clinical and Experimental Research, 18*(5), 1125-1132.

Jain, A., Concato, J., & Leventhal, J. M. (2002). How good is the evidence linking breastfeeding and intelligence? *Pediatrics, 109*(6), 1044-1053.

Janzen, L. A., Nanson, J. L., & Block, G. W. (1995). Neuropsychological evaluation of preschoolers with fetal alcohol syndrome. *Neurotoxicology and Teratology, 17*(3), 273-279.

Johnson, J., Im-Bolter, N., & Pascual-Leone, J. (2003). Development of mental attention in gifted and mainstream children: The role of mental capacity, inhibition, and speed of processing. *Child Development, 74*(6), 1594-1614.

Jones, K. L., & Smith, D. W. (1973). Recognition of the fetal alcohol syndrome in early infancy. *Lancet, 302*(7836), 999-1001.

Jones, K. L., Smith, D. W., Ulleland, C. N., & Streissguth, P. (1973). Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet, 1*(7815), 1267-1271.

Kable, J. A., & Coles, C. D. (2004). The impact of prenatal alcohol exposure on neurophysiological encoding of environmental events at six months. *Alcoholism, Clinical and Experimental Research, 28*(3), 489-496.

Kaemingk, K. L., Mulvaney, S., & Halverson, P. T. (2003). Learning following prenatal alcohol exposure: Performance on verbal and visual multitrial tasks. *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists, 18*(1), 33-47.

Kalberg, W. O., Provost, B., Tollison, S. J., Tabachnick, B. G., Robinson, L. K., Eugene Hoyme, H., . . . May, P. A. (2006). Comparison of motor delays in young children with fetal alcohol syndrome to those with prenatal alcohol exposure and with no prenatal alcohol exposure. *Alcoholism, Clinical and Experimental Research, 30*(12), 2037-2045

Kaplan-Estrin, M., Jacobson, S. W., & Jacobson, J. L. (1999). Neurobehavioral effects of prenatal alcohol exposure at 26 months. *Neurotoxicology and Teratology, 21*(5), 503-511.

Karapetsas, A.B., & Vlachos, F.M. (1997). Sex and handedness in development of visuomotor skills. *Perceptual and Motor Skills, 85,* 131-140.

Kartin, D., Grant, T. M., Streissguth, A. P., Sampson, P. D., & Ernst, C. C. (2002). Three-year developmental outcomes in children with prenatal alcohol and drug exposure. *Pediatric Physical Therapy : The Official Publication of the Section on Pediatrics of the American Physical Therapy Association, 14*(3), 145-153.

Kelly, S. J., Day, N., & Streissguth, A. P. (2000). Effects of prenatal alcohol exposure on social behavior in humans and other species. *Neurotoxicology and Teratology, 22*(2), 143-149.

Kerns, K. A., Don, A., Mateer, C. A., & Streissguth, A. P. (1997). Cognitive deficits in nonretarded adults with fetal alcohol syndrome. *Journal of Learning Disabilities, 30*(6), 685-693.

Khaole, N. C., Ramchandani, V. A., Viljoen, D. L., & Li, T. K. (2004). A pilot study of alcohol exposure and pharmacokinetics in women with or without children with fetal alcohol syndrome. *Alcohol and Alcoholism (Oxford, Oxfordshire), 39*(6), 503-508.

Kirksey, A., Wachs, T. D., Yunis, F., Srinath, U., Rahmanifar, A., McCabe, G. P., . . . Jerome, N. W. (1994). Relation of maternal zinc nutriture to pregnancy outcome and infant development in an egyptian village. *The American Journal of Clinical Nutrition, 60*(5), 782-792.

Klein, PS 2001, 'A Mediational Intervention for Sensitizing Caregivers (MISC)', in Klein, P 2001 (Ed) Seeds of Hope: Twelve Years of Early Intervention in Africa, Unipub forlag, Norway, pp29-93.

Kline, J., Shrout, P., Stein, Z., Susser, M., & Warburton, D. (1980). Drinking during pregnancy and spontaneous abortion. *Lancet, 2*(8187), 176-180.

Klug, M. G., Burd, L., Kerbeshian, J., Benz, B., & Martsolf, J. T. (2003). A comparison of the effects of parental risk markers on pre- and perinatal variables in multiple patient cohorts with fetal alcohol syndrome, autism, tourette syndrome, and sudden infant death syndrome: An enviromic analysis. *Neurotoxicology and Teratology, 25*(6), 707-717.

Knoesen, N. (2003). *An exploration of the relationship between the Revised Griffiths Scales and grade one scholastic development.* (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Knoesen, N. (2005). *Exploring the reliability and construct-related validity of the Locomotor Subscale of the Griffiths Mental Developmental Scales – Extended Revised (GMDS-ER).* (Unpublished doctoral thesis). Nelson Mandela Metropolitan University, Port Elizabeth, South Africa.

Kodituwakku, P. W. (2007). Defining the behavioral phenotype in children with fetal alcohol spectrum disorders: A review. *Neuroscience and Biobehavioral Reviews, 31*(2), 192-201.

Kodituwakku, P. W. (2010). A neurodevelopmental framework for the development of interventions for children with fetal alcohol spectrum disorders. *Alcohol (Fayetteville, N.Y.), 44*(7-8), 717-728.

Kodituwakku, P. W., Handmaker, N. S., Cutler, S. K., Weathersby, E. K., & Handmaker, S. D. (1995). Specific impairments in self-regulation in children exposed to alcohol prenatally. *Alcoholism, Clinical and Experimental Research, 19*(6), 1558-1564.

Kodituwakku, P. W., Kalberg, W., & May, P. A. (2001). Cognitive and behavioral effects of prenatal alcohol exposure. *Future Neurology, 6*(2), 237-259.

Kodituwakku, P. W., Segall, J.M., & Beatty, G. K. (2011). From research to practice: An integrative framework for the development of interventions for children with fetal alcohol spectrum disorders. *Neuropsychology Review, 21*(2), 204-223.

Kotras, N. (1998). *A revision of a section of the Hearing and Speech scales of the Griffiths Scales of Mental Development.* (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Kotras, N. (2003). *Exploring the construct validity of the Revised Extended Griffiths' Language Subscale in the British Isles.* (Unpublished doctoral thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Kovas, Y., Haworth, C. M., Dale, P. S., & Plomin, R. (2007). The genetic and environmental origins of learning abilities and disabilities in the early school years. *Monographs of the Society for Research in Child Development, 72*(3), vii, 1-144.

Kramer, M. S., Fombonne, E., Igumnov, S., Vanilovich, I., Matush, L., Mironova, E., . . . Promotion of Breastfeeding Intervention Trial (PROBIT) Study Group. (2008). Effects of prolonged and exclusive breastfeeding on child behavior and maternal adjustment: Evidence from a large, randomized trial. *Pediatrics, 121*(3), e435-40.

Krige, P. (1988). A physically handicapped child: A longitudinal study. In D. M. Luiz (Ed.), *Griffiths Scales of Mental Development: South African studies* (Research papers No. C.25) (pp.38-43). Port Elizabeth, South Africa.

Kruger, M.J.L. (1983). *'n Ondersoek na die verband tussen kronologiese ouderdom en die graad van skoolgereedheid.* Unpublished doctoral dissertation, University of South Africa.

Kuhn, D., & Siegler, R. S. (1998). Handbook of Child Psychology, (5th ed). Volume 2: Cognition, Perception and Language.

Lalloo, R.L. (1997). *The neuropsychological outcome of mild closed head injuries in children*. (Unpublished master's thesis). University of Durban-Westville. South Africa.

Larkby, C., & Day, N. (1997). The effects of prenatal alcohol exposure. *Alcohol Health and Research World, 21*(3), 192-198.

Larroque, B., Kaminski, M., Dehaene, P., Subtil, D., Delfosse, M. J., & Querleu, D. (1995). Moderate prenatal alcohol exposure and psychomotor development at preschool age. *American Journal of Public Health, 85*(12), 1654-1661.

Larrson, G., Bohlin, A. B., & Tunell, R. (1985). Prospective study of children exposed to variable amounts of alcohol in utero. *Archives of Diseases in Childhood,* 60, 316-321.

Laughton, B., Springer, P., Grove, D., Seedat, S., Cornell, M., Kidd, M., . . . Cotton, M. (2010). Longitudinal developmental profile of children from low socio-economic circumstances in cape town, using the 1996 griffiths mental development scales. *SAJCH : The South African Journal of Child Health, 4*(4), 106-111.

Lemoine, P., Harousseau, H., Borteyru, J.P., & Manuet, J.C. (1968). Les enfants des parents alcoholiques:anomalies observees a propos de 127 cas. *Quest Medical*, *25*, 476 – 487

Levine, S.C., Huttenlocher, J., Taylor, A., & Langrock, A. (1999). Early sex differences in spatial skill. *Developmental Psychology, 35(4)*, 940-949.

Lewis, S. J., Zuccolo, L., Davey Smith, G., Macleod, J., Rodriguez, S., Draper, E. S., . . . Gray, R. (2012). Fetal alcohol exposure and IQ at age 8: Evidence from a population-based birth-cohort study. *PloS One, 7*(11), doi: 10.1371/journal.pone.0049407.

Lidz, C. S. (2003). *Early Childhood Assessment*. John Wiley & Sons, Inc, Hoboken, New Jersey

Lindsley, T. A., Comstock, L. L., & Rising, L. J. (2002). Morphologic and neurotoxic effects of ethanol vary with timing of exposure in vitro. *Alcohol, 28*(3), 197-203.

Little, R.E., Graham, J.M., & Herman, H. (1982). Fetal Alcohol Effects in Humans and Animals, *Advances in Alcohol & Substance Abuse*, 1(3-4), 103-125.

Little, B. B., Snell, L. M., Rosenfeld, C. R., Gilstrap, L. C.,3rd, & Gant, N. F. (1990). Failure to recognize fetal alcohol syndrome in newborn infants. *American Journal of Diseases of Children (1960), 144*(10), 1142-1146.

Little, R. E., & Sing, C. F. (1987). Genetic and environmental influences on human birth weight. *American Journal of Human Genetics, 40*(6), 512-526.

Livy, D. J., Miller, E. K., Maier, S. E., & West, J. R. (2003). Fetal alcohol exposure and temporal vulnerability: Effects of binge-like alcohol exposure on the developing rat hippocampus. *Neurotoxicology and Teratology, 25*(4), 447-458.

Lombard, M. (1989). *The SETT and the Griffiths Scales of Mental Development: A correlative study*. (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Louw, D.A., & Edwards, D.J.A. 1997. Psychology: An introduction for students in Southern Africa, (2nd Ed). Heinemann Higher and Further Education Ltd.

Ludlow, A. R. (1980). Early intervention in Down‟s Syndrome [Letter to the editor]. *British Medical Journal*, *281*, 1143.

Ludlow, J. R., & Allen, L. M. (1979). The effect of early intervention and pre-school stimulus on the development of the down's syndrome child. *Journal of Mental Deficiency Research, 23*(1), 29-44.

Luiz, D. M. (1988a). *A battered child: A follow-up study*. In D. M. Luiz (Ed.), Griffiths Scales of Mental Development: South African studies (Research papers No. C25) (pp. 52-58). Port Elizabeth: University of Port Elizabeth.

Luiz, D. M. (1988b). *A child with a hearing loss: A longitudinal study*. In D. M. Luiz (Ed.), Griffiths Scales of Mental Development: South African studies (Research papers No. C25) (pp. 44-51). Port Elizabeth: University of Port Elizabeth.

Luiz, D. M. (1988c). *A comparative study of two scales of language development. The Reynell and Griffiths*. In D. M. Luiz (Ed.), Griffiths Scales of Mental Development: South African Studies (Research Paper No. C25) (pp.16-20). Port Elizabeth: University of Port Elizabeth.

Luiz, D. M. (1988d). *Developmental profiles of young children*. In D. M. Luiz (Ed.), Griffiths Scales of Mental Development: South African studies (Research papers No. C25) (pp. 33-38). Port Elizabeth: University of Port Elizabeth.

Luiz, D. M., Barnard, A., Knoesen, N.P., Kotras, N., McAlinden, P., & O' Connell,R. (2004). *Griffiths Mental Development Scales-Extended Revised (GMDS-ER). Administration Manual*. Association for Research in Infant and Child Development (ARICD): Amersham, UK.

Luiz, D.M., Foxcroft, C.D., & Povey, J. (2006). The Griffiths Mental Developmental Scales: A factorial validity study. *S Afr J Psychol*, *36*(1), 192–214.

Luiz, D. M., Foxcroft, C. D., Worsfold, N., Kotras, N., & Kotras, H. (2001). The Griffiths Scales of Mental Development: An evaluation of their prediction of scholastic achievement. *South African Journal of Education*, *21* (2), 81-83.

Luiz, D. M. & Heimes, L. (1994). The Junior South African Intelligence Scales and the Griffiths Scales of Mental Development: A correlative study. In R. Van Eeden, M. Robinson, & A. B. Posthuma (Eds.). *Studies on South African Intelligence Scales* (pp.2-13). Human Sciences Research Council (HSRC): Pretoria, South Africa.

Luiz, D. M., Foxcroft, C. D., & Stewart, R. (2001). The construct validity of the griffiths scales of mental development. *Child: Care, Health and Development, 27*(1), 73-83.

Maccoby, E.E., & Jacklin, C.N. (1974). *The psychology of sex differences*. Stanford, CA: Stanford University Press.

Maier, S. E., & West, J. R. (2001a). Drinking patterns and alcohol-related birth defects. *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism, 25*(3), 168-174.

Maier, S. E., & West, J. R. (2001b). Regional differences in cell loss associated with binge-like alcohol exposure during the first two trimesters equivalent in the rat. *Alcohol, 23*(1), 49-57.

Majewski, F. (1981). Alcohol embryopathy: Some facts and speculations about pathogenesis. *Neurobehavioral Toxicology and Teratology, 3*(2), 129-144.

Martin, R. P., Dombrowski, S. C., Mullis, C., Wisenbaker, J., & Huttunen, M. O. (2006). Smoking during pregnancy: Association with childhood temperament, behavior, and academic performance. *Journal of Pediatric Psychology, 31*(5), 490-500.

Martin, J. C., Martin, D. C., Sigman, G., & Radow, B. (1977). Offspring survival, development, and operant performance following maternal ethanol consumption. *Developmental Psychobiology, 10*(5), 435-446.

Matney, L. (1999). *Relationship of fitness and gross motor skills for five-to-six-year-old children*. Perceptual and Motor Skills, *89*, 739-747.

Mattson, S. N., Crocker, N., & Nguyen, T. T. (2011). Fetal alcohol spectrum disorders: Neuropsychological and behavioral features. *Neuropsychology Review, 21*(2), 81-101.

Mattson, S. N., Goodman, A. M., Caine, C., Delis, D. C., & Riley, E. P. (1999). Executive functioning in children with heavy prenatal alcohol exposure. *Alcoholism, Clinical and Experimental Research, 23*(11), 1808-1815.

Mattson, S. N., & Riley, E. P. (1998). A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcoholism, Clinical and Experimental Research, 22*(2), 279-294.

Mattson, S. N., & Riley, E. P. (2000). Parent ratings of behavior in children with heavy prenatal alcohol exposure and IQ-matched controls. *Alcoholism, Clinical and Experimental Research, 24*(2), 226-231.

Mattson, S. N., Riley, E. P., Gramling, L., Delis, D. C., & Jones, K. L. (1997). Heavy prenatal alcohol exposure with or without physical features of fetal alcohol syndrome leads to IQ deficits. *The Journal of Pediatrics, 131*(5), 718-721.

Mattson, S. N., Riley, E. P., Gramling, L., Delis, D. C., & Jones, K. L. (1998). Neuropsychological comparison of alcohol-exposed children with or without physical features of fetal alcohol syndrome. *Neuropsychology, 12*(1), 146-153.

Mattson, S. N., Riley, E. P., Sowell, E. R., Jernigan, T. L., Sobel, D. F., & Jones, K. L. (1996). A decrease in the size of the basal ganglia in children with fetal alcohol syndrome. *Alcoholism, Clinical and Experimental Research, 20*(6), 1088-1093.

Mattson, S. N., & Roebuck, T. M. (2002). Acquisition and retention of verbal and nonverbal information in children with heavy prenatal alcohol exposure. *Alcoholism, Clinical and Experimental Research, 26*(6), 875-882.

Mattson, S. N., Schoenfeld, A. M., & Riley, E. P. (2001). Teratogenic effects of alcohol on brain and behavior. *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism, 25*(3), 185-191.

May, P. A., Fiorentino, D., Coriale, G., Kalberg, W. O., Hoyme, H. E., Aragon, A. S., . . . Ceccanti, M. (2011). Prevalence of children with severe fetal alcohol spectrum disorders in communities near rome, italy: New estimated rates are higher than previous estimates. *International Journal of Environmental Research and Public Health, 8*(6), 2331-2351.

May, P. A., & Gossage, J. P. (2001). Estimating the prevalence of fetal alcohol syndrome. A summary. *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism, 25*(3), 159-167.

May, P. A., Gossage, J. P., Brooke, L. E., Snell, C. L., Marais, A. S., Hendricks, L. S., . . . Viljoen, D. L. (2005). Maternal risk factors for fetal alcohol syndrome in the western cape province of south africa: A population-based study. *American Journal of Public Health, 95*(7), 1190-1199.

May, P. A., Gossage, J. P., Marais, A. S., Adnams, C. M., Hoyme, H. E., Jones, K. L., . . . Viljoen, D. L. (2007). The epidemiology of fetal alcohol syndrome and partial FAS in a south african community. *Drug and Alcohol Dependence, 88*(2-3), 259-271.

May, P. A., Gossage, J. P., Marais, A. S., Hendricks, L. S., Snell, C. L., Tabachnick, B. G., . . . Viljoen, D. L. (2008). Maternal risk factors for fetal alcohol syndrome and partial fetal alcohol syndrome in south africa: A third study. *Alcoholism, Clinical and Experimental Research, 32*(5), 738-753.

May, P. A., Gossage, J. P., White-Country, M., Goodhart, K., Decoteau, S., Trujillo, P. M., Kalberg, W. O., Viljoen, D. L., & Hoyme, H. E. (2004). Alcohol Consumption and Other Maternal Risk Factors for Fetal Alcohol Syndrome among Three Distinct Samples of Women before, during, and after Pregnancy: The Risk Is Relative. *American Journal of Medical Genetics Part C,* 127C, 10-20.

May, P. A., Gossage, J. P., Smith, M., Tabachnick, B. G., Robinson, L. K., Manning, M., . . . Hoyme, H. E. (2010). Population differences in dysmorphic features among children with fetal alcohol spectrum disorders. *Journal of Developmental and Behavioral Pediatrics : JDBP, 31*(4), 304-316.

McCarver, D. G. (2001). ADH2 and CYP2E1 genetic polymorphisms: Risk factors for alcohol-related birth defects. *Drug Metabolism and Disposition: The Biological Fate of Chemicals, 29*(4 Pt 2), 562-565.

McCall, R. B. (1981). Nature-nurture and the two realms of development: A proposed integration with respect to mental development. *Child Development*, *52*, 1-12.

McGee, C. L., Bjorkquist, O. A., Riley, E. P., & Mattson, S. N. (2009). Impaired language performance in young children with heavy prenatal alcohol exposure. *Neurotoxicology and Teratology, 31*(2), 71-75.

Meisels, S. (1996). Charting the continuum of assessment and intervention. In S.Meisels & E. Fenichel (Eds.), *New vision for the developmental assessment of infants and young children*. Washington, DC: Zero to Three.

Mick, E., Biederman, J., Prince, J., Fischer, M. J., & Faraone, S. V. (2002). Impact of low birth weight on attention-deficit hyperactivity disorder. *Journal of Developmental and Behavioral Pediatrics : JDBP, 23*(1), 16-22.

Mills, J. L., Graubard, B. I., Harley, E. E., Rhoads, G. G., & Berendes, H. W. (1984). Maternal alcohol consumption and birth weight. how much drinking during pregnancy is safe? *JAMA : The Journal of the American Medical Association, 252*(14), 1875-1879.

Mistry, R. S., Biesanz, J. C., Taylor, L. C., Burchinal, M., & Cox, M. J. (2004). Family income and its relation to preschool children's adjustment for families in the NICHD study of early child care. *Developmental Psychology, 40*(5), 727-745.

Molteno, C.D. (1991). Psychomotor Development, in *Child Health for All: A Manual For Southern Africa*, edited by M.A.Kibel, & L.A. Wagstaff. Cape Town: Oxford University Press.

Moore, K. L., & Persaud, T. V. N. (1993). *The developing human.* USA: WB Saunders Company.

Moosajee, S. (2007). *Exploring the construct-related validity of the Personal-Social Subscale of the Griffiths Mental Developmental Scales – Extended Revised (GMDS-ER).* (Unpublished doctoral thesis). Nelson Mandela Metropolitan University, Port Elizabeth, Port Elizabeth, South Africa.

Mondschein, E.R., Adolph, K.E., & Tamis-LeMonda, C.S. (2000). Gender bias in mothers' expectations about infant crawling. *Journal of Experimental Child Psychology, 77,* 304-316.

Morisset, C.E., Barnard, K.E., & Booth, C.L. (1995). Toddlers' language development: Sex differences within social risk. *Developmental Psychology, 31,* 851-865.

Morojele, N. K., London, L., Olorunju, S. A., Matjila, M. J., Davids, A. S., & Rendall-Mkosi, K. M. (2010). Predictors of risk of alcohol-exposed pregnancies among women in an urban and a rural area of south africa. *Social Science & Medicine (1982), 70*(4), 534-542.

Morris, R.D (1996). Relationships and distinctions among the concepts of attention, memory and executive function: *A Developmental Perspective*. In G.R, Lyon & N. Krasnegor (Eds.). Attention, Memory, and Executive Function (pp.11-16). Baltimore, MD: Paul Brookes Publishing.

Mothuloe, V. B. (1990). *The Aptitude Test for Beginners and the Griffiths Scales of Mental development: An investigation into the assessment of the cognitive abilities of grade 1 children.* (Unpublished master's thesis). Medical University of South Africa, Pretoria, South Africa.

Murphy, K.R., & Davidshofer, C.O. (2001). Psychological Testing: Principles and Applications (5t^{h} ed). New Jersey: Prentice-Hall.

Naglieri, J.A., & Rojahn, J. (2001). Gender differences in Planning, Attention, Simultaneous, and Successive (PASS) cognitive processes and achievement. *Journal of Educational Psychology, 93(2),* 430-437.

Naidoo, S., Chikte, U., Laubscher, R., & Lombard, C. (2005). Fetal alcohol syndrome: Anthropometric and oral health status. *The Journal of Contemporary Dental Practice, 6*(4), 101-115.

Nanson, J. L., & Hiscock, M. (1990). Attention deficits in children exposed to alcohol prenatally. *Alcoholism, Clinical and Experimental Research, 14*(5), 656-661.

Newman, B., &Newman , P.(1987). Development through life: A psychosocial approach. Chicago, IL: Dorsey Press.

Neuspiel, D.R. (1994). Behavior in cocaine-exposed infants and children: Association versus causality. *Drug and Alcohol Dependence*, *36*, 101-107.

NICHD Early Child Care Research Network. (2003). Do children's attention processes mediate the link between family predictors and school readiness? *Developmental Psychology, 39*, 581-593.

Nuttall, E. V., Romero, I., & Kalesnik, J. (1992). *Assessing and Screening Preschoolers: Psychological and Educational Dimensions*. Boston: Allyn and Bacon.

O'Connor, M. J., Shah, B., Whaley, S., Cronin, P., Gunderson, B., & Graham, J. (2002). Psychiatric illness in a clinical sample of children with prenatal alcohol exposure. *The American Journal of Drug and Alcohol Abuse, 28*(4), 743-754.

Odendaal, H. J., Steyn, D. W., Elliott, A., & Burd, L. (2009). Combined effects of cigarette smoking and alcohol consumption on perinatal outcome. *Gynecologic and Obstetric Investigation, 67*(1), 1-8.

O'Hare, E. D., Lu, L. H., Houston, S. M., Bookheimer, S. Y., Mattson, S. N., O'Connor, M. J., & Sowell, E. R. (2009). Altered frontal-parietal functioning during verbal working memory in children and adolescents with heavy prenatal alcohol exposure. *Human Brain Mapping, 30*(10), 3200-3208.

O'Leary, C., Zubrick, S. R., Taylor, C. L., Dixon, G., & Bower, C. (2009). Prenatal alcohol exposure and language delay in 2-year-old children: The importance of dose and timing on risk. *Pediatrics, 123*(2), 547-554.

O'Leary, C. M. (2004). Fetal alcohol syndrome: Diagnosis, epidemiology, and developmental outcomes. *Journal of Paediatrics and Child Health, 40*(1-2), 2-7.

Olegard, R., Sabel, K. G., Aronsson, M., Sandin, B., Johansson, P. R., Carlsson, C., . . . Hrbek, A. (1979). Effects on the child of alcohol abuse during pregnancy. retrospective and prospective studies. *Acta Paediatrica Scandinavica.Supplement, 275*, 112-121.

Olson, H. C., Morse, B. A., & Huffine, C. (1998). Development and psychopathology: Fetal alcohol syndrome and related conditions. *Seminars in Clinical Neuropsychiatry, 3*(4), 262-284.

Osborn, J. A., Harris, S. R., & Weinberg, J. (1993). Fetal alcohol syndrome: Review of the literature with implications for physical therapists. *Physical Therapy, 73*(9), 599-607.

Parker, J. G., & Asher, S. R. (1987). Peer relationships and later personal adjustment. Are low-accepted children at risk? *Psychological Bulletin, 102,* 357-389.

Paton, S.J., & Croom, C.S. (2010). An overview of fetal alcohol spectrum disorders for physicians. *Primary Care Reports*, 1-15.

Parry, C.D.H. (2000). Alcohol problems in developing countries: challenges for the new millennium. *Suchtmed*, 2, 216-220.

Parnell, S. E., O'Leary-Moore, S. K., Godin, E. A., Dehart, D. B., Johnson, B. W., Allan Johnson, G., . . . Sulik, K. K. (2009). Magnetic resonance microscopy defines ethanol-induced brain abnormalities in prenatal mice: Effects of acute insult on gestational day 8. *Alcoholism, Clinical and Experimental Research, 33*(6), 1001-1011.

Parry, C. D. (2005). South Africa: Alcohol today. *Addiction (Abingdon, England), 100*(4), 426-429.

Pembrey, M. E., Bygren, L. O., Kaati, G., Edvinsson, S., Northstone, K., Sjostrom, M., . . . ALSPAC Study Team. (2006). Sex-specific, male-line transgenerational responses in humans. *European Journal of Human Genetics : EJHG, 14*(2), 159-166.

Piaget, J. (1952). *The Origins of Intelligence in Children.* Translated by Margaret Cook. New York: International Universities Press, Inc.

Piaget, J. (1963). *The Origins of Intelligence.* NY: W. W. Norton and Company, Inc.

Pierce, D. R., & West, J. R. (1986). Alcohol-induced microencephaly during the third trimester equivalent: Relationship to dose and blood alcohol concentration. *Alcohol (Fayetteville, N.Y.), 3*(3), 185-191.

Piper, M. C., & Pless, I. B. (1980). Early intervention for infants with down syndrome: A controlled trial. *Pediatrics, 65*(3), 463-468.

Plant, M.L. (1985). Women, Drinking and Pregnancy. New York: Tavistock Publications.

Poikolainen, K., Leppanen, K., & Vuori, E. (2002). Alcohol sales and fatal alcohol poisonings: A time-series analysis. *Addiction, 97*(8), 1037-1040.

Pollitt, E. (2000). A developmental view of the undernourished child: Background and purpose of the study in pangalengan, indonesia. *European Journal of Clinical Nutrition, 54 Suppl 2*, S2-10.

Povey, J.L. (2008). *Exploring the Construct-Related Validity of the Eye and Hand Coordination Subscale of the Griffiths Mental Developmental Scales-Extended Revised (GMDS-ER).* (Unpublished doctoral thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Quattlebaum, J. L., & O'Connor, M. J. (2012). Higher functioning children with prenatal alcohol exposure: Is there a specific neurocognitive profile? *Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence,* doi: 10.1080/09297049.2012.713466

Rasmussen, C. (2005). Executive functioning and working memory in fetal alcohol spectrum disorder. *Alcoholism, Clinical and Experimental Research, 29*(8), 1359-1367.

Rasmussen, C., Horne, K., & Witol, A. (2006). Neurobehavioral functioning in children with fetal alcohol spectrum disorder. *Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence, 12*(6), 453-468.

Rasmussen, C., Wyper, K., & Talwar, V. (2009). The relation between theory of mind and executive functions in children with fetal alcohol spectrum disorders. *The Canadian Journal of Clinical Pharmacology, 16*(2), e370-80.

Reinisch, J.M., & Sanders, S.A. (1992). Prenatal hormonal contributions to sex differences in human cognitive and personality development. In A.A. Gerall, H. Moltz, & I.L. Ward (Eds.), *Handbook of behavioural neurology: Vol. 11. Sexual differentiation* (pp. 221-243). New York: Plenum Press.

Richards, M., Hardy, R., Kuh, D., & Wadsworth, M. E. (2002). Birthweight, postnatal growth and cognitive function in a national UK birth cohort. *International Journal of Epidemiology, 31*(2), 342-348.

Richardson, G. A., & Day, N. L. (1991). Maternal and neonatal effects of moderate cocaine use during pregnancy. *Neurotoxicology and Teratology, 13*(4), 455-460.

Riikonen, R., Salonen, I., Partanen, K., & Verho, S. (1999). Brain perfusion SPECT and MRI in foetal alcohol syndrome. *Developmental Medicine and Child Neurology, 41*(10), 652-659.

Riley, E. P., Infante, M. A., & Warren, K. R. (2011). Fetal alcohol spectrum disorders: An overview. *Neuropsychology Review, 21*(2), 73-80.

Riley, E. P., Mattson, S. N., Sowell, E. R., Jernigan, T. L., Sobel, D. F., & Jones, K. L. (1995). Abnormalities of the corpus callosum in children prenatally exposed to alcohol. *Alcoholism, Clinical and Experimental Research, 19*(5), 1198-1202.

Riley, E. P., & McGee, C. L. (2005). Fetal alcohol spectrum disorders: An overview with emphasis on changes in brain and behavior. *Experimental Biology and Medicine (Maywood, N.J.), 230*(6), 357-365.

Robinson, M., Oddy, W. H., McLean, N. J., Jacoby, P., Pennell, C. E., de Klerk, N. H., . . . Newnham, J. P. (2010). Low-moderate prenatal alcohol exposure and risk to child behavioural development: A prospective cohort study. *BJOG: An International Journal of Obstetrics and Gynaecology, 117* (9), 1139-1150.

Roebuck, T. M., Mattson, S. N., & Riley, E. P. (1998). A review of the neuroanatomical findings in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcoholism, Clinical and Experimental Research, 22*(2), 339-344.

Roebuck, T. M., Mattson, S. N., & Riley, E. P. (2002). Interhemispheric transfer in children with heavy prenatal alcohol exposure. *Alcoholism, Clinical and Experimental Research, 26*(12), 1863-1871.

Roebuck, T. M., Simmons, R. W., Mattson, S. N., & Riley, E. P. (1998). Prenatal exposure to alcohol affects the ability to maintain postural balance. *Alcoholism, Clinical and Experimental Research, 22*(1), 252-258.

Roebuck-Spencer, T. M., & Mattson, S. N. (2004). Implicit strategy affects learning in children with heavy prenatal alcohol exposure. *Alcoholism, Clinical and Experimental Research, 28*(9), 1424-1431.

Rome-Flanders, T., & Cronk, C. (1995). A longitudinal study of infant vocalizations during mother-infant games. *Journal of Child Language, 22,* 259-274.

Rosett, H. L. (1980). A clinical perspective of the fetal alcohol syndrome. *Alcoholism, Clinical and Experimental Research, 4*(2), 119-122.

Rosett, H. L., Weiner, L., Lee, A., Zuckerman, B., Dooling, E., & Oppenheimer, E. (1983). Patterns of alcohol consumption and fetal development. *Obstetrics and Gynecology, 61*(5), 539-546.

Rosnow, R., & Rosenthal, R. (1996). *Beginning Behavioural Research*. Englewood Cliffs,N.J.: Prentice-Hall

Roussotte, F. F., Bramen, J. E., Nunez, S. C., Quandt, L. C., Smith, L., O'Connor, M. J., . . . Sowell, E. R. (2011). Abnormal brain activation during working memory in children with prenatal exposure to drugs of abuse: The effects of methamphetamine, alcohol, and polydrug exposure. *Neuroimage, 54*(4), 3067-3075.

Rubin, P. C., Craig, G. F., Gavin, K., & Sumner, D. (1986). Prospective survey of use of therapeutic drugs, alcohol, and cigarettes during pregnancy. *British Medical Journal (Clinical Research Ed.), 292*(6513), 81-83.

Rutter, M. (1979). Protective factors in children's responses to stress and disadvantage. In M. W. Kent & J. E. Rolf (Ed.), *Primary prevention of psychopathology* (Vol. 3, pp. 49-74). Hanover, NH: University Press of New England.

Rydz, D., Shevell, M. I., Majnemer, A., & Oskoui, M. (2005). Developmental screening. *Journal of Child Neurology, 20*(1), 4-21.

Rye, H.(2001). 'Twelve Years of Early Intervention Studies in Ethiopia', in Klein, P (Ed) Seeds of Hope: Twelve Years of Early Intervention in Africa, Unipub forlag, Norway.

Saarni, C., Mumme, D. L., & Campos, J. J. (1998). Emotional development: action, communication, and understanding. In N. Eisenberg (Ed.), *Handbook of Child Psychology,* (5th ed). *Volume 3: Social, Emotional, and Personality Development.* (pp. 237-310). New York: John Wiley & Sons, Inc.

Salman, M. S., Sharpe, J. A., Eizenman, M., Lillakas, L., To, T., Westall, C., . . . Steinbach, M. J. (2006). Saccadic adaptation in children. *Journal of Child Neurology, 21*(12), 1025-1031.

Sandison, A. (2005). *Exploring the developmental profile of black HIV positive/AIDS infants and children: A longitudinal study.* (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Santrock, J. W. (2002). *Life span development* (8th ed.). NY: McGraw-Hill College.

Sameroff, A. J., Seifer, R., Baldwin, A., & Baldwin, C. (1993). Stability of intelligence from preschool to adolescence: The influence of social and family risk factors. *Child Development, 64*(1), 80-97.

Sameroff, A. J., Seifer, R., Barocas, R., Zax, M., & Greenspan, S. (1987). Intelligence quotient scores of 4-year-old children: Social-environmental risk factors. *Pediatrics, 79*(3), 343-350.

Sampson, P. D., Streissguth, A. P., Bookstein, F. L., & Barr, H. M. (2000). On categorizations in analyses of alcohol teratogenesis. *Environmental Health Perspectives, 108 Suppl 3*, 421-428.

Samson, H. H. (1986). Microcephaly and fetal alcohol syndrome: human and animal studies. *Alcohol and brain development*, 167-183.

Sandberg, A. D., Nyden, A., Gillberg, C., & Hjelmquist, E. (1993). The cognitive profile in infantile autism--a study of 70 children and adolescents using the griffiths mental development scale. *British Journal of Psychology, 84 (Pt 3)*(Pt 3), 365-373.

Segall, M. H., Dasen, P. R., Berry, J. W. & Poortinga, Y. (1999). *Human Behavior in Global Perspective: An Introduction to Cross-cultural Psychology* (2nd ed.). Boston*:* Allyn & Bacon.

Schonfeld, A. M., Paley, B., Frankel, F., & O'Connor, M. J. (2006). Executive functioning predicts social skills following prenatal alcohol exposure. *Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence, 12*(6), 439-452.

Schneider, W., & Bjorklund, D. F. (1998). Memory. In D. Kuhn & R. S. Siegler (Eds.), *Handbook of Child Psychology,* (5th ed). Volume 2: Cognition, Perception and Language. (pp. 1-50). New York: John Wiley.

Schul, R., Stiles, J., Wulfeck, B., & Townsend, J. (2004). How 'generalized' is the 'slowed processing' in SLI? The case of visuospatial attentional orienting. *Neuropsychologia, 42*(5), 661-671.

Schuler, M. E., Nair, P., & Harrington, D. (2003). Developmental outcome of drug-exposed children through 30 months: A comparison of bayley and bayley-II. *Psychological Assessment, 15*(3), 435-438.

Shaywitz, S. E., Caparulo, B. K., & Hodgson, E. S. (1981). Developmental language disability as a consequence of prenatal exposure to ethanol. *Pediatrics, 68*(6), 850-855.

Shenkin, S. D., Starr, J. M., & Deary, I. J. (2004). Birth weight and cognitive ability in childhood: A systematic review. *Psychological Bulletin, 130*(6), 989-1013.

Shonkoff, J. P., & Phillips, D. A. (Eds.). (2000). From Neurons to Neighbourhoods: The Science of Early Childhood. Development Committee on Integrating the Science of Early Childhood Development. Washington D.C.: National Academy Press.

Short, A. (1987). A critical appraisal of cognitive programmes for preschool children. In O. Van den Berg & T. Vergnani (Eds.), *Door to the future: The preschool child in South Africa* (pp. 57-83). Bellville: University of the Western Cape.

Silva, A., Metha, Z., & O'callaghan, F. J. (2006). The relative effect of size at birth, postnatal growth and social factors on cognitive function in late childhood. *Annals of Epidemiology, 16*(6), 469-476.

Singleton, R., Straits, B.C., Straits, M.M., & McAllister, R.J. (1988). Approaches to Social Research. New York: Oxford University Press.

Sirin, S.R. (2005). *Socioeconomic status and academic achievement: A meta-analytic review of research*. Rev Educ Res, *75*(3), 417-453.

Skinner, B.F. (1957). Verbal behavior. New York: Appleton-Century-Crofts.

Smith, J. A., Bidder, R. T., Gardner, S. M., & Gray, O. P. (1980). Griffiths scales of mental development and different users. *Child: Care, Health and Development, 6*(1), 11-16.

Smith, R. A., Sibert, J. R., & Harper, P. S. (1990). Early development of boys with duchenne muscular dystrophy. *Developmental Medicine and Child Neurology, 32*(6), 519-527.

Sobell, L. C., Agrawal, S., Annis, H., Ayala-Velazquez, H., Echeverria, L., Leo, G. I., . . . Zioikowski, M. (2001). Cross-cultural evaluation of two drinking assessment instruments: Alcohol timeline followback and inventory of drinking situations. *Substance use & Misuse, 36*(3), 313-331.

Sood, B., Delaney-Black, V., Covington, C., Nordstrom-Klee, B., Ager, J., Templin, T., . . . Sokol, R. J. (2001). Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. dose-response effect. *Pediatrics, 108*(2), E34.

Spain, B. (1970). Spina Bifida survey. *Quarterly Bulletin of the Intelligence Unit of the Greater London Council*, *12*, 5-13.

Sowell, E. R., Jernigan, T. L., Mattson, S. N., Riley, E. P., Sobel, D. F., & Jones, K. L. (1996). Abnormal development of the cerebellar vermis in children prenatally exposed to alcohol: Size reduction in lobules I-V. *Alcoholism, Clinical and Experimental Research, 20*(1), 31-34.

Stanton, M. E., & Goodlett, C. R. (1998). Neonatal ethanol exposure impairs eyeblink conditioning in weanling rats. *Alcoholism, Clinical and Experimental Research, 22*(1), 270-275.

Steinhausen, H. C. (1995). Children of alcoholic parents. A review. *European Child & Adolescent Psychiatry, 4*(3), 143-152.

Stewart, R. (2005). *The Griffiths Scales of Mental Development: Proposed new items for the revision of Subscales A, B, C, D and E.* (Unpublished Doctoral thesis), Nelson Mandela Metropolitan University.

Stoler, J. M., & Holmes, L. B. (2004). Recognition of facial features of fetal alcohol syndrome in the newborn. *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics, 127C*(1), 21-27.

Stoler, J. M., Ryan, L. M., & Holmes, L. B. (2002). Alcohol dehydrogenase 2 genotypes, maternal alcohol use, and infant outcome. *The Journal of Pediatrics, 141*(6), 780-785.

Stratton, K., Howe, C., & Battaglia, F. (1996). *Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention and Treatment*. Washington D.C: National Academy Press.

Streissguth, A. (1997). *Fetal Alcohol Syndrome. A guide for families and communities.* Baltimore: Paul H. Brookes Publishing Co.

Streissguth, A. P., Aase, J. M., Clarren, S. K., Randels, S. P., LaDue, R. A., & Smith, D. F. (1991). Fetal alcohol syndrome in adolescents and adults. *JAMA : The Journal of the American Medical Association, 265*(15), 1961-1967.

Streissguth, A., Barr, H., Kogan, J., & Bookstein, F. (1996). *Understanding the Occurrence of Secondary Disabilities in Clients With Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE):* Final Report for Center for Disease Control & Prevention. Seattle: University of Washington.

Streissguth, A. P., Barr, H. M., Sampson, P. D., & Bookstein, F. L. (1994). Prenatal alcohol and offspring development: The first fourteen years. *Drug and Alcohol Dependence, 36*(2), 89-99.

Streissguth, A. P., Clarren, S. K., & Jones, K. L. (1985). Natural history of the fetal alcohol syndrome: A 10-year follow-up of eleven patients. *Lancet, 2*(8446), 85-91.

Streissguth, A. P., & Dehaene, P. (1993). Fetal alcohol syndrome in twins of alcoholic mothers: Concordance of diagnosis and IQ. *American Journal of Medical Genetics, 47*(6), 857-861.

Streissguth, A. P., & O'Malley, K. (2000). Neuropsychiatric implications and long-term consequences of fetal alcohol spectrum disorders. *Seminars in Clinical Neuropsychiatry, 5*(3), 177-190.

Streissguth, A. P., Randels, S. P., & Smith, D. F. (1991). A test-retest study of intelligence in patients with fetal alcohol syndrome: Implications for care. *Journal of the American Academy of Child and Adolescent Psychiatry, 30*(4), 584-587.

Streissguth, A. P., Barr, H. M., Martin, D. C., & Herman, C. S. (1980). Effects of maternal alcohol, nicotine, and caffeine use during pregnancy on infant mental and motor development at eight months. *Alcoholism, Clinical and Experimental Research, 4*(2), 152-164.

Sulik, K. K. (2005). Genesis of alcohol-induced craniofacial dysmorphism. *Experimental Biology and Medicine, 230*(6), 366-375.

Sulik, K. K., Johnston, M. C., & Webb, M. A. (1981). Fetal alcohol syndrome: Embryogenesis in a mouse model. *Science , 214*(4523), 936-938.

Sullivan, W. C. (1899). A note on the influence of maternal inebriety on the offspring. *Journal of Mental Science, 45*, 489–503.

Swayze, V. W.,2nd, Johnson, V. P., Hanson, J. W., Piven, J., Sato, Y., Giedd, J. N., . . . Andreasen, N. C. (1997). Magnetic resonance imaging of brain anomalies in fetal alcohol syndrome. *Pediatrics, 99*(2), 232-240.

Sweeney, K. (1994). *Cluster analysis of the Griffiths profiles of a white South African clinical population*. (Unpublished Master's thesis), University of Port Elizabeth.

Tamura, T., Goldenberg, R. L., Johnston, K. E., & Chapman, V. R. (2004). Relationship between pre-pregnancy BMI and plasma zinc concentrations in early pregnancy. *The British Journal of Nutrition, 91*(5), 773-777.

Thomas, J.R., & French, K.E. (1985). Gender differences across age in motor performance: A meta-analysis. *Psychological Bulletin, 98,* 260-282.

Thomas, S. E., Kelly, S. J., Mattson, S. N., & Riley, E. P. (1998). Comparison of social abilities of children with fetal alcohol syndrome to those of children with similar IQ scores and normal controls. *Alcoholism, Clinical and Experimental Research, 22*(2), 528-533.

Thompson, R. A., & Raikes, H. A. (2006). The social and emotional foundations of school readiness. In J. Knitzer, R. Kaufmann & D. Perry (Eds.), *Early childhood Mental Health*. Baltimore, MD: Paul H. Brookes Publishing Co.

Tomlinson-Keasey, C. (1985). *Child Development. Psychological, Sociocultural and Biological Factors.* Illnois: The Dorsey Press.

Townes, B.D., Trupin, E.W., & Fay, G. (1980). Neuropsychological correlates of academic performance. *Academic Psychology Bulletin, 2,* 189-199.

Tozzi, A. E., Bisiacchi, P., Tarantino, V., Chiarotti, F., D'Elia, L., De Mei, B., . . . Salmaso, S. (2012). Effect of duration of breastfeeding on neuropsychological development at 10 to 12 years of age in a cohort of healthy children. *Developmental Medicine and Child Neurology, 54*(9), 843-848.

Tukulu, A. N. (1996). *The Denver II Scale and the Griffiths Scales of Mental Development: A correlative study.* (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Uauy, R., & De Andraca, I. (1995). Human milk and breast feeding for optimal mental development. *The Journal of Nutrition, 125*(8 Suppl), 2278S-2280S.

Uauy, R., & Peirano, P. (1999). Breast is best: Human milk is the optimal food for brain development. *The American Journal of Clinical Nutrition, 70*(4), 433-434.

Uecker, A., & Nadel, L. (1996). Spatial locations gone awry: Object and spatial memory deficits in children with fetal alcohol syndrome. *Neuropsychologia, 34*(3), 209-223.

Urban, M., Chersich, M. F., Fourie, L. A., Chetty, C., Olivier, L., & Viljoen, D. (2008). Fetal alcohol syndrome among grade 1 schoolchildren in northern cape province: Prevalence and risk factors. *South African Medical Journal, 98*(11), 877-882.

Valenzuela, C. F., Lindquist, B., & Zamudio-Bulcock, P. A. (2010). A review of synaptic plasticity at purkinje neurons with a focus on ethanol-induced cerebellar dysfunction. *International Review of Neurobiology, 91*, 339-372.

Van Der Leeden, M., Van Dongen, K., Kleinhout, M., Phaff, J., De Groot, C. J., De Groot, L., & Hesseling, P. B. (2001). Infants exposed to alcohol prenatally: Outcome at 3 and 7 months of age. *Annals of Tropical Paediatrics, 21*(2), 127-134.

Van Rooyen, K. (2005). *The performance of South African and British children on the Griffiths Mental Development Scales- extended revised: a comparative study*. (Unpublished master's thesis). Nelson Mandela Metropolitan University, Port Elizabeth, South Africa.

Viljoen, D., Croxford, J., Gossage, J. P., Kodituwakku, P. W., & May, P. A. (2002). Characteristics of mothers of children with fetal alcohol syndrome in the western cape province of south africa: A case control study. *Journal of Studies on Alcohol, 63*(1), 6-17.

Viljoen, D. L., Gossage, J. P., Brooke, L., Adnams, C. M., Jones, K. L., Robinson, L. K., . . . May, P. A. (2005). Fetal alcohol syndrome epidemiology in a south african community: A second study of a very high prevalence area. *Journal of Studies on Alcohol, 66*(5), 593-604.

Veena, S. R., Krishnaveni, G. V., Wills, A. K., Kurpad, A. V., Muthayya, S., Hill, J. C., . . . Srinivasan, K. (2010). Association of birthweight and head circumference at birth to cognitive performance in 9- to 10-year-old children in south india: Prospective birth cohort study. *Pediatric Research, 67*(4), 424-429.

Vygotsky, L.S. (1978). Mind in Society: *The Development of Higher Mental Process*. In M. Cole V, John-Steiner, S. Scribner S & E. Souberman, E (Eds.). Harvard University Press, UK.

Vygotsky, L.S. (1986). *Thought and language*. Cambridge, MA: MIT Press (original work published in 1934).

Walker, S. P., Wachs, T. D., Gardner, J. M., Lozoff, B., Wasserman, G. A., Pollitt, E., . . . International Child Development Steering Group. (2007). Child development: Risk factors for adverse outcomes in developing countries. *Lancet, 369*(9556), 145-157.

Ward, N. (1997). *The use of the Denver II Scales and the Griffiths Scales of Mental Development with South African, Coloured, pre-school children.* (Unpublished master's thesis). University of Port Elizabeth, Port Elizabeth, South Africa.

Warner, R. H., & Rosett, H. L. (1975). The effects of drinking on offspring: An historical survey of the american and british literature. *Journal of Studies on Alcohol, 36*(11), 1395-1420.

Warren, K. R., Calhoun, F. J., May, P. A., Viljoen, D. L., Li, T. K., Tanaka, H., . . . Mundle, G. (2001). Fetal alcohol syndrome: An international perspective. *Alcoholism, Clinical and Experimental Research, 25*(5 Suppl ISBRA), 202S-206S.

Welbourn, H. (1975). Spina bifida children attending ordinary schools. *British Medical Journal, 1*(5950), 142-145.

Weinberg, J. (1992). Prenatal ethanol effects: Sex differences in offspring stress responsiveness. *Alcohol, 9*(3), 219-223.

West, J. R. (1986). Long-term effects of developmental exposure to alcohol. *Neurotoxicology, 7*(2), 245-256.

West, J. R., & Goodlett, C. R. (1990). Teratogenic effects of alcohol on brain development. *Annals of Medicine, 22*(5), 319-325.

West, J. R., Goodlett, C. R., Bonthius, D. J., Hamre, K. M., & Marcussen, B. L. (1990). Cell population depletion associated with fetal alcohol brain damage: Mechanisms of BAC-dependent cell loss. *Alcoholism, Clinical and Experimental Research, 14*(6), 813-818.

Whaley, S. E., O'Connor &, M. J., & Gunderson, B. (2001). Comparison of the adaptive functioning of children prenatally exposed to alcohol to a non-exposed clinical sample. *Alcoholism, Clinical and Experimental Research, 25*(7), 1018-1024.

Willford, J. A., Richardson, G. A., Leech, S. L., & Day, N. L. (2004). Verbal and visuospatial learning and memory function in children with moderate prenatal alcohol exposure. *Alcoholism, Clinical and Experimental Research, 28*(3), 497-507.

Wilsnack, S. C., Klassen, A. D., Schur, B. E., & Wilsnack, R. W. (1991). Predicting onset and chronicity of women's problem drinking: A five-year longitudinal analysis. *American Journal of Public Health, 81*(3), 305-318.

Wisniewski, K., Dambska, M., Sher, J. H., & Qazi, Q. (1983). A clinical neuropathological study of the fetal alcohol syndrome. *Neuropediatrics, 14*(4), 197-201.

WHO *Improving Mother/child Interaction to Promote Better Psychosocial Development in Children, Program on Mental Health*, viewed in March, 2010, www.who.int/mental_health/media/en/29.pdf

WHO *Global strategy for infant and young child feeding.* (A54/INF.DOC./4), viewed in May 2010, http://www.who.int/nutrition/topics/infantfeeding_recommendation/en/index.html

Wolmarans P., Langenhoven, M., & Faber, M. (1993). *Food, Facts and Figures*. Cape Town: Oxford University Press.

Woodward, A. L., & Markman, E. M. (1998). Early word learning. In D. Kuhn & R. S. Siegler (Eds.), *Handbook of Child Psychology,* (5th ed). *Volume 2: Cognition, Perception and Language.* (pp. 1-50). New York: John Wiley.

.

List of Appendices

APPENDIX A: Ethics Clearance and Department of Health Approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)
Ref: R14/49 Viljoen

CLEARANCE CERTIFICATE **PROTOCOL NUMBER** M01-11-20

PROJECT The Prevention of Fetal Alcohol Syndrome In De Aar, Northern Cape Province of South Africa

INVESTIGATORS Prof D Viljoen

DEPARTMENT School of Pathology, SAIMR

DATE CONSIDERED 01-11-09

DECISION OF THE COMMITTEE *

Approved unconditionally

DATE 01-11-21 **CHAIRMAN** .....(Professor P E Cleaton-Jones)

* Guidelines for written "informed consent" attached where applicable.

c c Supervisor: Prof D Viljoen
Dept of School of Pathology, SAIMR

W:\e2\eln0015\HumEth97.wdb\M 01-11-20

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee.

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Leigh-Anne F Davies

CLEARANCE CERTIFICATE	**M090222**
PROJECT	Fetal Alcohol Spectrum Disorder: A Longitudinal Neurodevelopmental Study of Children from Infancy to 5 Years of Age using the Griffiths.....
INVESTIGATORS	Ms Leigh-Anne F Davies.
DEPARTMENT	Psychology Department
DATE CONSIDERED	09.02.27
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 09.03.23 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof K Cockcroft

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

.....

DEPARTMENT OF HEALTH

LEFAPHA LA BOITEKANELO

ISEBE NWEZEMPILO

DEPARTEMENT VAN GESONDHEID

Market Square
Private Bag X5049
KIMBERLEY
8300

Isakhiwo Sephondo
Market Square
Private Bag X5049
KIMBERLEY
8300

Tel (053) 8300621

Market Square
Kgetsanaposo X5049
KIMBERLEY
8300

PoskantoorGebou
Markplein
Privaatsak X5049
KIMBERLEY
8300

Fax (053) 8334394

Enquiries : L Magwentshu-Napoles
Olpatlisiso :
Imibuzo :
Navrae :

Reference :
Tshupelo :
Isalathiso :
Verwysings :

Date : 09 March 2000
Leshupelo :
Umhla :
Datum :

Ms Pat Craig
School of Pathology
University of the Witwatersrand
Johannesburg

RE: FETAL ALCOHOL SYNDROME STUDY - NORTHERN CAPE

The department appreciates your research support and hereby grants you permission to continue with the study.

We would like to note, as indicated in your letter, that you will provide all the financial and human resources needed for the study. The department will not be in a position to assist with these resources.

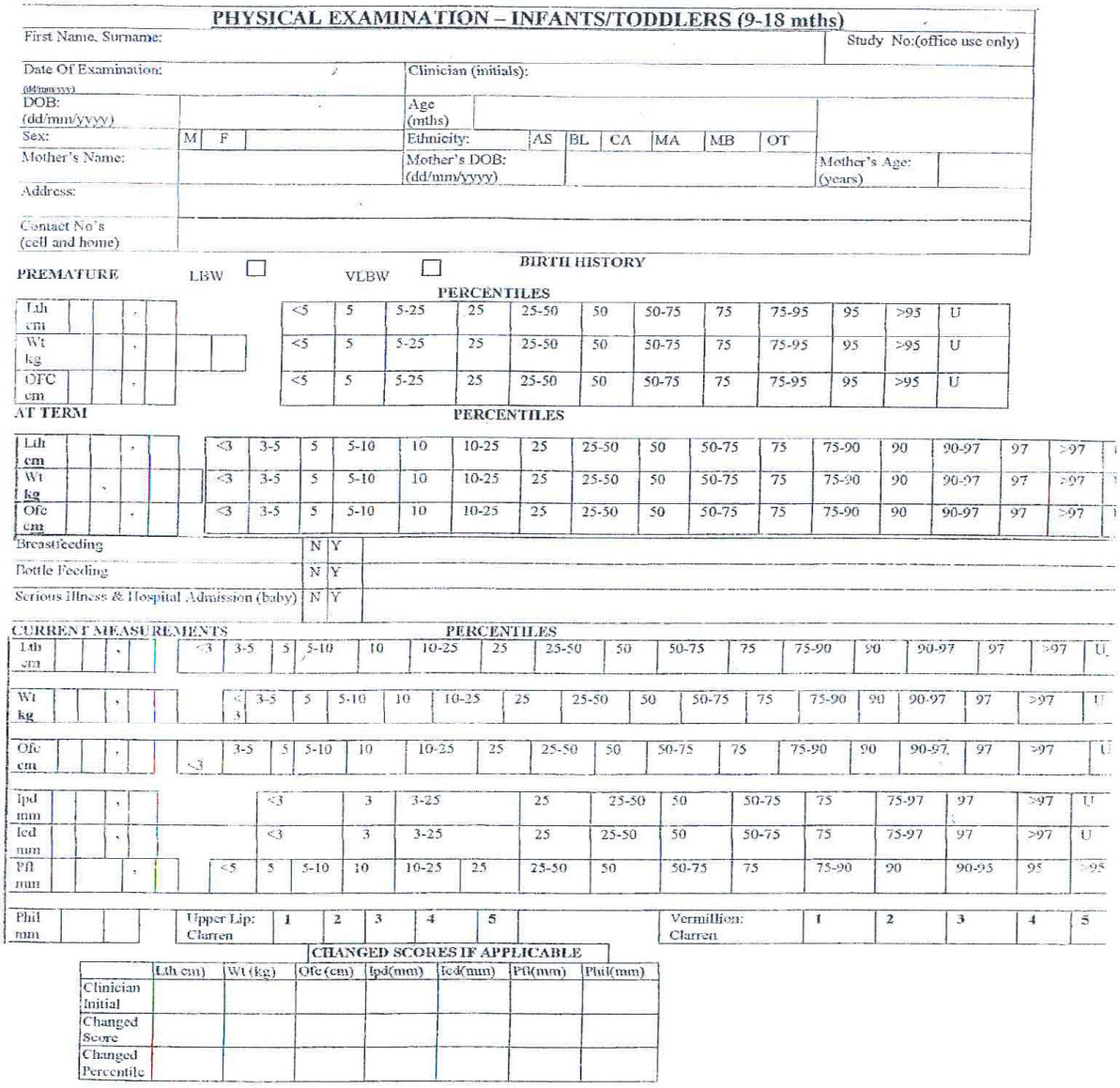
We also request that you communicate with our Information and Communication Unit through Ms Jeanette Hunter, for feedback on the study. Her contact number is (053) 8300784.

Thank you!

DEPUTY DIRECTOR-GENERAL

Cc Ms Jeanette Hunter, Information and Communication
Ms Carvie Madikane, MWCH

APPENDIX B: Clinical Examination and Consent Forms



PHYSICAL EXAMINATION – INFANTS/TODDLERS (9-18 mths)

First Name. Surname:												Study No:(office use only)	
Date Of Examination: (dd/mm/yyy)				Clinician (initials):									
DOB: (dd/mm/yyyy)				Age (mths)									
Sex:	M	F		Ethnicity:	AS	BL	CA	MA	MB	OT			
Mother's Name:				Mother's DOB: (dd/mm/yyyy)							Mother's Age: (years)		
Address:													
Contact No's (cell and home)													

PREMATURE LBW ☐ VLBW ☐ BIRTH HISTORY

PERCENTILES

Lth cm	<5	5	5-25	25	25-50	50	50-75	75	75-95	95	>95	U
Wt kg	<5	5	5-25	25	25-50	50	50-75	75	75-95	95	>95	U
OFC cm	<5	5	5-25	25	25-50	50	50-75	75	75-95	95	>95	U

AT TERM

PERCENTILES

Lth cm	<3	3-5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-97	97	>97	
Wt kg	<3	3-5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-97	97	>97	
Ofc cm	<3	3-5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-97	97	>97	

Breastfeeding	N	Y
Bottle Feeding	N	Y
Serious Illness & Hospital Admission (baby)	N	Y

CURRENT MEASUREMENTS

PERCENTILES

Lth cm	<3	3-5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-97	97	>97	U	
Wt kg	<3	3-5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-97	97	>97	U	
Ofc cm	<3	3-5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-97	97	>97	U	
Ipd mm	<3		3	3-25		25	25-50	50	50-75	75	75-97	97	>97	U				
Icd mm	<3		3	3-25		25	25-50	50	50-75	75	75-97	97	>97	U				
Pfl mm	<5	5	5-10	10	10-25	25	25-50	50	50-75	75	75-90	90	90-95	95	>95			

Phil mm	Upper Lip: Clarren	1	2	3	4	5		Vermillion: Clarren	1	2	3	4	5

CHANGED SCORES IF APPLICABLE

	Lth cm)	Wt (kg)	Ofc (cm)	Ipd(mm)	Icd(mm)	Pfl(mm)	Phil(mm)
Clinician Initial							
Changed Score							
Changed Percentile							

		Normal	Abnormal
Neurological			
Gross Motor	Sitting (unsupported)		
	Weight-bearing		
	Walking		
Fine-Motor:	Pincer Grip		
	Stacks blocks		
Vision:	Light/Dark		
	Red Reflex		
	Overall		
Hearing:	Overall		
Cranium:			
Fontanelle:			
Face:	General		
	Ears		
	Eyes		
	Nose		
	Mouth		
Neck:			
Thorax:			
Heart:			
Limbs:			
Hands:	General		
	Creases		
	Dermal patterns		
Feet:			
Skin:			
Hair:			
Other:			
Comments:			

Y	N	SCORE	
		1	HEIGHT (10th or below)
		2	WEIGHT (10th or below)
		3	HEAD CIRCUMFERENCE (10th or below)
		1	GROSS MOTOR
		1	FINE MOTOR
			ABNORMAL BEHAVIOUR
		2	MIDFACIAL HYPOLASIA
		1	RAILROAD TRACK EARS
		3	PALPEBRAL FISSURE LENGTH
		0	STRABISMUS
		2	PTOSIS
		1	EPICANTHAL FOLDS
		1	FLAT NASAL BRIDGE
		2	ANTEVERTED NARES
		2	LONG PHILTRUM
		3	SMOOTH PHILTRUM
		3	THIN VERMILION BORDER UPPER LIP
		0	PROGNATHISM CARDIAC MURMUR
		1	CARDIAC MALFORMATION
		2	SUPINATION OF ELBOW
		1	CLINODACTYLY OF 5TH FINGERS
		1	CAMPTODACTYLY
		1	HOCKEY STICK PALMAR CREASES
		0	HYPERTRICHOSIS
		1	HIRSUTISM
		0	HYPOPLASTIC NAILS
		35	

DIAGNOSIS

Abnormalities compatible with FASD (mark box that apply)

1. ☐ Growth deficiency
2. ☐ Structural abnormality
3. ☐ Cognitive/behavioral abnormalities
4. ☐ No abnormalities compatible with FASD observed

Does the child have FASD?

☐ NO

If Yes (Please Specify)

☐ FAS
☐ PARTIAL FAS
☐ ARND
☐ ARBD

Does the child have another Diagnosis?

☐ No
☐ Yes (please specify)

_____
_____
_____

Is special follow-up or testing recommended?

☐ No
☐ Yes (please specify)

_____
_____
_____

Notes: _____
_____

MATERNAL INFORMATION:

Height (in cm, to one decimal place)				,		
Weight (in kg, to nearest half kg)				,		
OFC (in cm, to one decimal place)				,		
MUAC (in cm, to one decimal place)				,		

CLINICIAN INITIAL	

Dear Mrs _____ January 2002

Professor Denis Viljoen and his team have conducted research studies to determine the incidence of Fetal Alcohol Syndrome (FAS) in the Western Cape, Gauteng and Northern Cape provinces. As part of the second part of the project in the Northern Cape, a medical survey of all babies born in 2002-2003 will be carried out.

FAS is the most common preventable cause of mental retardation worldwide. It can cause mental retardation, behavioural difficulties (such as hyperactivity and poor concentration span) and problems with the child's growth.

This study is part of a larger research programme to determine previously undetected (hidden) medical problems suggestive of disorders such as fetal alcohol syndrome. These may include minor heart defects, physical abnormalities, ear and eye defects and others.

Each baby will be measured for length, weight and head circumference and will be examined by doctors during clinics to be held at the Joan Wertheim Centre from 2002-2005. Babies identified to undergo clinical examination will be required to partially undress to enable doctors to listen to their hearts. No specimens or samples will be taken during the initial screening. A number of babies may be required to have developmental tests, which consist of watching your baby play and his/her responses to toys and other harmless items, administered by a psychologist/psychometrist (a person specially trained to tests baby's development). You will be able to sit in for both the clinical and developmental assessments. Participation in this study is entirely voluntary and there is no charge for either the clinical or developmental assessments.

Should you wish for your baby to take part, we ask you to please sign the attached consent form. This form should be returned to Mrs Mabel Nero, the FAS Community Co-ordinator. Further information may be obtained by contacting Ms Leigh-Anne Fourie on (011)489-9509 or faspr@nhls.ac.za. Consent may be withdrawn at any time of the study. Please note that we undertake to refer all babies to the relevant medical authorities should problems be found. If developmental tests reveal any difficulties, that may affect your baby's progress, we will inform you, and refer to relevant specialists for issues to be addressed.

We realize that this programme will take up some of your time, so all participating mothers will be given a food voucher and a colour, family photograph.

We look forward to your participation and thank you for your co-operation.

Yours Sincerely,

Ms Leigh-Anne Fourie

Project Co-ordinator

Consent Form

Yes, I ……... **mother/guardian** of

……..... (**Child's name**) give permission for him/her to be clinically examined by the doctors. I also give permission for my child to undergo a developmental assessment, should it be required.

Mother's address (place where the child lives)

……

……

Childs Date of Birth (day/month/year)

……....

Name of mother (if different from above)

……

Contact telephone number ……

Signature of mother/guardian

……

Date ……...

PHYSICAL EXAMINATION

Name: _____ Number: _____

School's Name: _____

Date of Examination: / / Examiner: _____

D.O.B.: / / Age: _____ years/months

Sex: _____

Ht	_____	Ht %	_____
Wt	_____	Wt %	_____
OFC	_____	OFC %	_____
PFL	_____	PFL %	_____

Upper Lip Length _____

Mental status/behaviour _____

Neurological _____

Cranium _____

Face: General _____

Ears _____

Eyes _____

Nose _____

Mouth _____

Neck _____

Thorax _____

Heart _____

Arms _____

Hands: General _____

Creases _____

Dermal Patterns _____

Legs: _____

Feet: _____

Skin: _____

Hair: _____

Other/ Comments _____

_____

_____

Mother's Name _____

Address: _____

_____

Tel. No. _____

Encircle scores if positive:

HT	(1)
WT	(2)
OFC	(3)
PFL	(3)
HYPERACT	(3)
FINEMOTR + GROSS MOTR	(3)
HYPOFACE	(2)
RREARS	(2)
STRABISM	(2)
PTOSIS	(3)
EPICANTH	(1)
NALSBRDG	(1)
ANTENARE	(1)
LONGPHIL	(3)
SMTHPHIL	(3)
NRRWRML	(3)
PROGNATH	(2)
HEARTMUR	(3)
SUPINATE	(3)
CLINDACT	(1)
CAMPDACT	(2)
PALMCR	(1)
HYPRTRIC	(2)
TOTAL:	50

DIAGNOSIS

Abnormalities compativle with FAS (check ALL that apply)

1. Growth deficency
2. Structural abnormality
3. Cognitive/behavioural abnormalities
4. No abnormalities compatible with FAS observed
5. No significant abnormalities of any kind observed

Does the Child have FAS or FASD?

1. No
2. Yes
3. High Dysmorphology Score

Does the Child have another diagnosis?

1. No
2. Yes (please specify)

a) _____

b) _____

c) _____

d) _____

Is special follow-up or testing recommended?

1. No
2. Yes (please specify)

_____

_____

_____

_____

_____

Notes: _____

_____

_____

_____

_____

_____

_____

_____

Dear Mrs _____ January 2007

As you are aware, 4 years ago you participated in the Phase 1 Prevention study conducted by the Foundation for Alcohol Related Research (FARR), in which a medical survey of all babies born in 2002-2003 was carried out. This study is a longitudinal follow-up of that larger research programme, to track your child's development and clinically re-examine them to detect medical problems suggestive of disorders such as fetal alcohol syndrome.

Each child, now age 5 years of age, will clinically be examined by doctors during clinics to be held at the Joan Wertheim Centre from 2007. No specimens or samples will be taken during the initial screening. Children will then be required to have a developmental test, similar to the ones that were done as infants administered by a psychologist/psychometrist (a person specially trained to tests baby's development). You will be able to sit in for both the clinical and developmental assessments. Participation in this study is entirely voluntary and there is no charge for either the clinical or developmental assessments.

Should you wish for your child to take part, we ask you to please sign the attached consent form and return it to Mrs Sylvia Swarts, the FAS Community Co-ordinator. Further information may be obtained by contacting Ms Leigh-Anne Fourie on (011) 489-9509 or faspr@nhls.ac.za. Consent may be withdrawn at any time of the study. Please note that we undertake to refer all children to the relevant medical authorities should problems be found. If developmental tests reveal any difficulties, that may affect your child's development, we will inform you, and refer to relevant specialists for issues to be addressed.

We realize that this programme will take up some of your time, so all participating mothers will be given a food voucher and children will be given a stationery pack.

We look forward to your participation and thank you for your co-operation.

Yours Sincerely,

Ms Leigh-Anne Fourie

Project Co-ordinator

Consent Form

Yes, I …….. **mother/guardian** of

……..... (**Child's name**) give permission for him/her to be clinically re-examined at 5 years old by the doctors. I also give permission for my child to undergo a developmental assessment.

Mother's address (place where the child lives)

……

……

Childs Date of Birth (day/month/year)

……....

Name of mother (if different from above)

……

Contact telephone number ……

Signature of mother/guardian

……

Date ……..

APPENDIX C: Maternal Interview and Consent Form

MATERNAL RISK FACTORS INTERVIEW
MOEDERLIKE RISIKO ONDERHOUD

OBJECTIVES

- To collect data on alcohol use during pregnancy to assist in diagnosing children with FASD
- To identify women who are currently exposed to alcohol who are at risk of producing a child with FASD
- To establish perceptions of milestones associated with early childhood development from caregivers with and without FASD

INSTRUCTIONS FOR INTERVIEWER

1. Where possible, study participants should personally enter the date on the informed consent.

2. If study participant is unable to read and/or write, the interviewer may read the consent form to the study participant. Participants giving consent should indicate this with either a signature or an X. The interview can then be read to the study participant, giving options only as indicated in the interview.

3. For some questions more than one answer may apply, select the option which **best** describes the participant's response; unless the questions indicates that more than one option may apply.

4. Complete the questionnaire in black ink. If errors occur while completing the questionnaire, make a single line through the error, and date and initial next to the correction. Do not obscure the original entry.

5. Calculations of the total drinks and developmental milestone questions can be made after the interview has been completed.

6. Circle the appropriate choice and in some cases place number within the box. Should the participant be unsure mark the relevant block.

3. MATERNAL RISK FACTORS AND DEVELOPMENTAL MILESTONE INTERVIEW / MOEDERLIKE RISIKO ONDERHOUD

Informed consent

Thank you for agreeing to participate in the study, before we begin I would like to give you an opportunity to officially consent to being a participant. This study is a follow-up study on the children and mothers we examined, assessed and interviewed four years ago, during a prevention study focusing on Fetal Alcohol Syndrome. In order to understand your child's development, we need to ask **you** some questions about the pregnancy, your health, and also about habits such as smoking and smoking. We would also like to ask you some questions relating to early childhood development. It may be difficult for you to remember some of these things but please try to give accurate information, if you don't remember, please tell me so I can record that. Whatever information you provide will be kept strictly confidential and will not be shown to other persons. Your name will never be mentioned to anyone outside the study without your consent. Participation in this survey is voluntary and you can now choose to answer each question and participate in the study. Should you not wish to partcipate, you will not be victimised in anyway.

Do you understand what I have said? Yes ☐ No ☐

Is there anything you want to ask me about this research?

If Yes, record questions:

_____

_____

Are you willing to be a particpant in this study, and do I have your permission to begin with the questionnaire? Yes ☐ No ☐

Full name _____ Date_____

Signature _____

Onderhoud toestemming

Ons doen navorsing oor fetale alkohol sindroom. Ons probeer vasstel watter faktore belangrik is vir 'n vrou om 'n gesonde baba te hê. Ek gaan vir jou vrae vra oor jou swangerskappe, jou familie, en vrae omtrent jou rook-en drinkgewoontes. Dit mag vir jou moeilik wees om van hierdie dinge te onthou of om daaroor te praat. Van die inligting mag van `n sensitiewe aard wees en ook moeilik wees om oor te praat. Ek wil jou egter verseker dat alles wat jy ons vertel baie vertroulik hanteer sal word. Jou naam sal nooit aan enige ander persoon bekend gemaak word sonder jou toestemming nie. Deelname aan die navorsing is vrywillig en as daar vrae is wat jy nie wil beantwoord nie is die jou keuse om dit nie te doen nie.

Is daar enige iets wat jy wil vra voordat ons begin?

Verstaan jy dit wat ek aan jou verduidelik het? Ja ☐ Nee ☐

Het ek jou toestemming om met die vraelys te begin? Ja ☐ Nee ☐

Volle naam _____

Handtekening _____

SECTION 1: PERSONAL DETAILS

1. Child's study no: ☐☐☐☐☐☐☐☐

2. Mother's name: _____ _____ _____
First name Middle name Last name

3. Mother's DOB: ☐☐☐☐/☐☐/☐☐
yyyy mm dd (1911/11/11 Unknown/onbekend)

4. Child's name: _____ _____ _____
First name Middle name Last name

5. Child's DOB: ☐☐☐☐/☐☐/☐☐
yyyy mm dd (1911/11/11 Unknown/onbekend)

6. Interviewee's relationship with the child? ..... ☐☐

1 = Child's Mother / Moeder
2 = Child's Father / Vader
3 = Sister / Suster
4 = Brother / Broer
5 = Mother's former husband or partner/vorige man/vriend
6 = Mother's friend / Vriend
7 = Aunt / Tannie
8 = Uncle / Oom
9 = Grandmother / Ouma
10 = Grandfather / Oupa
11 = Other / Ander (specify-spesifiseer)_____
88 = Unknown / Onbekend

7. Name of respondent (if interviewee is not the child's mother):

_____ _____ _____
First name Middle name Last name

8. Is this a **Proxy interview**:.....Yes ☐ No ☐
If **Yes**, please follow questions with **(*)**

9. Name and signature of interviewer:

_____ _____
Name Signature

10. Date of interview: ☐☐☐☐/☐☐/☐☐
yyyy mm dd (1911/11/11 Unknown / onbekend)

SECTION 2: DEMOGRAPHICS

1. What is your current marital status?

Wat is jou huwelikstatus? ..... ☐☐

1 = Married / getroud
2 = Widowed / weduwee
3 = Divorced / geskei
4 = Separated / vervreemd
5 = Single / enkel
6 = Unmarried, living with partner / ongetroud, woon saam met die pa van die kind
88 = Unknown / onbekend

2. To which ethnic group do you belong? (circle all that apply)

Aan watter etniese group behoort jy? (merk alles van toepassing)..... ☐☐

1 = Coloured / kleurling
2 = San
3 = Zulu
4 = Tswana
5 = Xhosa
6 = Venda
7 = Tsonga
8 = Sesotho
9 = Pedi
10 = Ndebele
11 = Swati
12 = Indian / Indies
13 = Afrikaaner Whiite/Blanke
14 = Engels White/Blanke
15 = Other, specify / Ander, spesifiseer_____

3. ***What was the highest grade or standard you passed?*** ☐☐ Grade

Watter graad of standerd het jy op skool voltooi? ☐☐ Standard

(enter 99 if school was never attended)

SECTION 3: SOCIO-ECONOMIC CIRCUMSTANCES

1. **What is your current employment status?.**

Wat is jou huidige werkstatus? ..... ☐☐

1 = Full time / voltyds (25 + hrs / week)
2 = Part time / deeltyds (<25 hrs / week)
3 = Seasonal, full time / seisoenwerker, voltyds
4 = Seasonal, part time / seisoenwerker, deeltyds
5 = Casual worker, part time / deeltydse werker
6 = Unemployed / werkloos
7 = Unemployed because of disability / werkloos agv ongeskiktheid
8 = Homemaker (at own home) / huisvrou
88 = Unknown/Don't know / onbekend/geen inligting

2. What kind of work do you do (if currently unemployed, what work did you do in the past)?

Watter tipe werk doen jy? ..... ☐☐

1 = Factory worker / fabriekswerk
2 = Farm worker / plaaswerk
3 = Office worker / kantoorwerk
4 = Domestic worker (cleaning or childcare) / huishulp(skoonmaak/kinders oppas)
5 = Homemaker (at own home) / huisvrou
6 = Informal Trader / straatverkoper
7 = Crafts person or artist / kunstenaar
8 = Professional (i.e. nurse, teacher) / professioneel (verpleegster, onderwyser)
9 = Commercial Sex Worker / sekswerker
10 = Other (specify) / ander (spesifiseer) _____
88 = Unknown/Don't know / onbekend/geen inligting
99 = Never worked / werkloos

SECTION 4: REPRODUCTIVE HEALTH

1. ***Are you currently using contraception (family planning)?***

   Gebruik jy nou enige voorbehoedmiddels (gesinsbeplanning)?**.....** ☐☐

   1 = Yes / Ja 2 = No / Nee 88 = Unknown / Onbekend

2. ***If no, why are you not currently using contraception?***

   Indien jy nie huidiglik voorbehoeding gebruik nie, hoekom nie? **.....** ☐☐

   1 = Not currently sexually active / nie huidiglik seksueel aktief nie
   2 = Trying to become pregnant / wil graag 'n kind hê
   3 = No longer fertile / vrou onvrugbaar
   4 = Partner had a vasectomy / man/kêrel het vasektomie gehad
   5 = Currently pregnant / huidiglik swanger
   6 = Do not have the money for contraception / nie geld vir voorbehoedmiddels nie
   7 = The family planning clinic does not provide a good service / gesinsbeplanning klinieke gee nie goeie diens nie
   8 = Going to the family planning clinic makes me feel uncomfortable / ek voel ongemaklik om gesinsgeplannings kliniek toe te gaan
   9 = Don't have transport to the clinic / geen vervoer om by kliniek te kom nie
   10 = Problems with side effects from contraception / newe-effekte van voorbehoedmiddels
   11 = My partner does not want me to use contraception / man/kêrel wil nie hê ek moet voorbehoedmiddels gebruik nie
   12 = Trading partner pays more if don't condomize / kry meer geld as ek nie 'n kondoom gebruik nie
   13 = Religious prohibition / deur geloof verbied
   14 = Have under gone a tubal ligation
   15 = Other (specify) / ander _____
   88 = Unknown / onbekend

3. ***What contraception are you currently using (if not currently using contraception, what was the last method you used)?***

   Wat se voorbehoedmiddel gebruik jy (indien nie huidig gebruik - die laaste keer wat 'n voorbehoedmiddel gebruik is, wat was gebruik?)**.....** ☐☐

   1 = Depo injection / inspuiting
   2 = Pill / die pil
   3 = Condoms / kondome
   4 = IUD / IUD
   5 = Other, specify / ander, spesifiseer _____
   88 = Unknown / onbekend
   99 = NA, undergone a tubal ligation

4. ***Please help me record the date all births, stillbirths, miscarriages or abortions, prior to, including and after, the child of interest.***

   Voltooi die table. Skryf die geboortedatum, stillgeboortes, miskrame, aborsies en gesondheid van all die lewende geboortes neer.

Order of pregnancy Swanger-skappe	*How did pregnancy end? Hoe het swangerskap geiendig?* *1 = Live birth / lewende baba* *2 = Stillbirth / still bebore* *3 = Miscarriage / miskraam* *4 = Induced Abortion / aborsie* *88 = Unknown / onbekend*	*Date pregnancy ended/ Einde van swangerskap Datum (yyyy/mm) 1911/11 =Unknown/onbekend*	*Health status of live births Gesondheid v lewende baba* *1 = alive / lewend* *2 = dead / dood* *88 = Unknown / onbekend*
1.		/	
2.		/	
3.		/	
4.		/	
5.		/	
6.		/	
7.		/	

To which ethnic group does/did the father of (child's name) belong (circle all that apply)?

Aan watter etniese group behoort die pa van (naam van kind)?..... ☐☐

1 = Coloured / kleurling
2 = San
3 = Zulu
4 = Tswana
5 = Xhosa
6 = Venda
7 = Tsonga
8 = Sesotho
9 = Pedi
10 = Ndebele
11 = Swati
12 = Indian / Indies
13 = Afrikaaner Whiite/Blanke
14 = Engels White/Blanke
15 = Other, specify / Ander, spesifiseer_____

88 = Unknown / onbekend

How many months were you pregnant with (child's name) when you found out you were pregnant?

Hoeveel maande was jy swanger met (naam van kind) toe jy uitgevind het jy is swanger?

..... ☐.☐ mths

88 = Unknown / onbekend

7. ***Did you have any health problems during your pregnancy that required hospitalisation or other treatment? (circle all that apply and specify as appropriate)***

Het jy enige gesondheids probleme gedurende you swangerskap gehad waarvoor jy in die hospitaal was of waarvoor jy behandeling ontvang het?

1 = Hypertension/hoë bloeddruk
2 = Gestational diabetes/Suikersiete in swangerskap
3 = IDDM diabetes/Insulien afhanklike suikersiekte
4 = Excessive nausea, vomiting/Erge naarheid, braking
5 = Vaginal bleeding/Vaginale bloeding
6 = Virus infections (chicken pox, measles, rubella)/Virus infeksies (waterpokkies, masels, duitse masels)
7 = High fever/Hoë koors
8 = Sexually transmitted diseases/Seksueel oordraagbare siektes
specify/spesifiseer _____
9 = Other acute infectious disease/Ander infeksies
specify/spesifiseer _____
10 = Other chronic health problems/Ander kroniese gesondheids probleme
specify/spesifiseer _____
11 = Preterm labour/Vroeë kraam
88 = Unknown/Onbekend
99 = NA, no health problems/NVT, geen gesondheids probleme

7. ***Did you take any medication prescribed by a doctor, nurse, or traditional healer during your pregnancy with (child's name)?***

Het jy medisyne wat deur 'n dokter, verpleegster of tradisionele dokter voorgeskryf was gebruik gedurende jou swangerskap met (naam van kind)? ..... ☐☐

1 = Yes / Ja 2 = No / Nee 88 = Unknown/cannot remember / Weet nie/kan nie onthou nie

<u>If yes</u>, specify what medication the mother took?
<u>Indien Ja</u>, wat het jy gebruik en waarvoor was dit?

_____
_____

9. ***After (child's name) was born, did you breastfeed?***

Na die geboorte van hierdie kind, het jy die baba geborsvoed? ..... ☐☐

1 = Yes / Ja 2 = No / Nee 88 = Unknown / weet nie/ kan nie onthou nie

10. ***If yes, for about how long did you do so?***

Indien jy hierdie kind geborsvoed het, vir hoe lank het jy dit gedoen?..... ☐☐ mths

88 = Unknown / onbekend

SECTION 5 – SMOKING

1. **When last did you smoke or use tobacco, including snuff or chewing tobacco?*

   Wanneer het jy laas gerook, gesnuif of tabak gekou?..... ☐☐

   1 = Currently smoke or use tobacco / rook or gebruik tabak huidig
   2 = Within the last 30 days / in die afgelope 30 dae
   3 = Within the last 12 months / in die afgelope 12 maande
   4 = More than a year ago / meer as 'n jaar gelede
   5 = Never / nooit
   8 = Cannot remember/don't know / kan nie onthou nie, weet nie

2. **How many cigarettes per day do you currently use (or did you use when you smoked regularly)?*

   Toe jy gerook en/of tabak en snuif gebruik het, hoeveel het jy gebruik?..... ☐☐

   88 = Cannot remember/don't know / kan nie onthou nie, weet nie 99 = NA , never smoked– NVT

3. **Did you smoke cigarettes or use tobacco, including snuff or chewing tobacco during your pregnancy with (child's name)?*

   Het jy sigarette of tabak gerook gedurende jou swangerskap met hierdie kind?..... ☐☐

   1 = Yes / Ja 2 = No / Nee
   88 = unknown/cannot remember/don't know / kan nie onthou nie, weet nie 99 = NA, never smoked / NVT

   If 'Yes', how many cigarettes per day did you use during your pregnancy with (child's name)?
   Indien 'JA', hoeveel sigarette het jy per dag gerook gedurende jou swangerskap met (kind se naam)?..... ☐☐

   88 = Unknown/Cannot remember / kan nie onthou nie, weet nie 99 = NA / NVT

SECTION 6: ROLE OF ALCOHOL IN WOMEN'S LIFE

1. When was the last time you had an alcoholic drink?

Wanneer laas het jy 'n drankie gedrink? ☐☐

1 = Within the last week / in die afgelope week
2 = Within the last 30 days / in die afgelope 30 dae
3 = Within the last 12 months / in die afgelope 12 maande
4 = More than a year ago / meer as 'n jaar gelede
88 = Unknown / onbekend
99 = NA, never drank / NVT, nog nooit gedrink nie

2. *How often do you drink?

Hoe gereeld drink jy? ☐☐

1 = Every day / elke dag
2 = Almost every day / amper elke dag
3 = Usually, one or two days a week / gewoonlik een of twee keer 'n week
4 = Usually, two or three times a month / gewoonlik twee of drie keer 'n maand
5 = About once a month / een keer 'n maand
6 = Several times a year / verskeie kere in 'n jaar
7 = At most, once a year / op die meeste, een keer 'n jaar
8 = Never / nooit
88 = Unknown, or not sure / onbekend/onseker

3. When do you usually drink? (cross all the boxes that apply)

Wanneer drink jy gewoonlik?

	Friday	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday
1. In the morning (before 12 noon) only/ slegs in die oggend (voor 12 uur)							
2. In the afternoon (12-6pm) only slegs in die middag (12-6pm)							
3. In the evening (6pm till late) only slegs in die aand (6pm tot laat)							
4. Mornings and afternoon oggend en middag							
5. Afternoon and evening middag en aand							
6. Throughout the day die hele dag							

4. ***For each day of the week, please tell me your usual beverage and how much alcohol you drink***
Vir elke dag van die week, vertel asb vir my wat jy gewoonlik drink en hoeveel, alcohol jy gewoonik drink

Interviewer: *specify amount in ml. A bottle usually contains 750 ml. A 2-liter plastic sack contains 2000 ml. A 'standard drink' is 1 can of beer (340 ml), 1 glass of wine (150 ml), 1 mixed drink ("cocktail"), or 1 shot of liquor*

	Beer Bier		Wine Wyn		Sweet Wine (sjerrie, port, muscadel)		Spirits Spiritus (likeur, mengeldrankies)		Homebrew (Napshushu)		Other Ander, specify _____	
	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink
Friday												
Saturday/ Saterdag												
Sunday/ Sondag												
Monday/ Maandag												
Tuesday/ Dinsdag												
Wednesday/ Woensdag												
Thursday/ Donderdag												
Total Drinks (ml)												

88 = Not sure / doesn't know – nie seker nie/weet nie 99 = NA, doesn't drink – NVT, drink nie

5. ***I understand that it may be difficult to remember what and how much you may have drank 5 years ago, but I would like to ask you some questions about drinking while you were pregnant with (child's name).***
Nou wil ek jou vra oor jou drinkgewoontes toe jy swanger was met (naam van kind).

8. For each day of the week, please tell me your usual beverage and how much alcohol you remember drinking during pregnancy.
Vir elke dag van die week, vertel asb vir my wat jy gewoonlik gedrink het en die hoeveelheid van alkohol wat jy kan onthou wat gedrink was gedurende swangerskap.

Interviewer: *specify amount in ml. A bottle usually contains 750 ml. A 2-liter plastic sack contains 2000 ml. A 'standard drink' is 1 can of beer (340 ml), 1 glass of wine (150 ml), 1 mixed drink ("cocktail"), or 1 shot of liquor.*

	Beer Bier		Wine Wyn		Sweet Wine (sjerrie, port, muscadel)		Spirits Spiritus (likeur, mengeldrankies)		Homebrew (Napshushu)		Other Ander, specify _____	
	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink	No. of drinks	ml. per drink
Friday/ Vrydag												
Saturday/ Saterdag												
Sunday/ Sondag												
Monday/ Maandag												
Tuesday/ Dinsdag												
Wednesday/ Woensdag												
Thursday/ Donderdag												
Total drink (ml)												

88 = Not sure / doesn't know – nie seker nie/weet nie

99 = NA, did not drink during pregnancy – NVT, drink nie

7. ***Would you like support, counselling or help with your drinking?***

Sou jy graag hulp wou hê met jou drankprobleem?**.....** ☐☐

1 = Yes / Ja
2 = No / Nee

88 = Unknown/cannot remember / onbekend/kannie onthou
99 = NA, does not drink / NVF drink nie

SECTION 7: FASD KNOWLEDGE

1. ***Did you ever get information that alcohol can harm a child during pregnancy?***

Het jy al ooit inligting gekry dat alkohol tydends swangerskap 'n kind kan benadeel?

..... ☐☐

1 = Yes / Ja
2 = No / Nee
88 = Unknown/cannot remember / onbekend/kannie onthou
99 = NA / NVT

If Yes **from**:
Indien Ja, van:

From nurses at antenatal clinic / verpleegsters by voorgeboorte kliniek..... ☐☐

On the TV or radio / oor die radio of op TV..... ☐☐

On a poster / op 'n plakaat..... ☐☐

If yes, where were the posters and which TV/radio station did they get information from?
Indien ja, waar was die plakaat en op watter TV/radio stasie het jy die inligting gekry?

_____
_____
_____
_____

SECTION 8: NUTRITION

1. ***Is your current weight similar to just before you became pregnant with (child's name)?***

   Is jou huidige gewig dieselfde as wat dit was net voor jy swanger geraak het met (naam van kind)

   ..... ☐☐

   1 = Much less / baie minder
   2 = About the same / omtrent dieselfde
   3 = Much more / baie meer
   88 = Unknown/cannot remember / onbekend/kan nie onthou

2. ***Were there times during the pregnancy when you didn't have enough food, if so how long did it usually last?***

   Was daar tye gedurende die swangerskap wat jy nie genoeg kos gehad nie, indien daar was hoe lank het die aangehou?**.....** ☐☐

   1 = For a day / vir n dag
   2 = For a week / vir a week
   3 = For a month or more / vir n maaand of meer
   4 = All the time / heeltyd
   88 = Unknown/doesn't know / weet nie of kannie onthou
   99 = NA, never hungry / NVT, nooit honger

4. ***Since (child's name) was born, have you had any health problems which required hospitalisation or other treatment?***
   Het jy enige gesondheids probleme gehad, vanaf (naam van die kind) se geboorte, waarvoor jy in die hospitaal opgeneem is of waarvoor jy ander behandeling ontvang het?**.....** ☐☐

   1 = Yes / Ja
   2 = No / Nee
   88 = Unknown/Don't know / weet nie
   99 = NA / NVT

5. ***<u>If yes</u>, specify the problem:***

   <u>Indien ja</u>, spesifiseer die probleem:

   _____ _____

6. ***Have you ever had TB treatment?***

   Het jy al ooit TB gehad?**.....** ☐☐

   1 = Yes / Ja
   2 = No / Nee
   88 = Unknown / onbekend

7. ***<u>If yes</u>, when was TB detected?***

   <u>Indien Ja</u>, het jy TB gehad?**.....** ☐☐☐☐/☐☐
   (1911/11 Unknown/onbekend)

Complete the woman's measurements

8. What is woman's height? ..... ☐☐☐.☐cm
   Wat is vrou se lengte?

9. What is woman's weight? ..... ☐☐☐.☐kg
   Wat is vrou se gewig?

10. What is woman's head circumference? ..... ☐☐.☐cm
    Wat is vrou se kopomtrek?

11. Does the woman have braids or very thick hair? ..... ☐☐
    Het die vrou gevlegde of baie dik hare?

    1 = Yes-Ja
    2 = No-Nee
    88 = Unknown/Don't know- weet nie
    99 = NA – NVT

SECTION 9: DEVELOPMENTAL MILESTONE PERCEPTIONS

The following section focuses on the milestones associated with infancy and early childhood development. Each statement has three possible choices but only 1 answer applies.

Eg: Ask the participant, "At which age do you think babies lift their heads up when lying on their stomach?" 6 months; 6-12 months or 12-18months old?

Record the participant's choice by circling the number in the relevant category.

Naam:

Verwantskap met kind							
Ouderdom	15-19	20-24	25-29	30-34	35-49	50-54	55+
Huweliks status	Bly saam	Getroud/Verloof	Enkel	Weduwee	Geskei		
Woon Area							
Opvoedkundige vlak	Geen primer	Primer voltooi	Onvolledige Hoer	Hoer voltooi	Tertier		
Hoeveelheid kinders opgevoed							
Beroep	Werkloos	Deeltys werksaam	Voltyds werksaam				

Baba	0-6m	6-12m	12-18m	Onbek	Totaal
Growwe Motories					
Lig kop op as hy/sy le	1	2	3	99	
Kruip op hande en knee	1	2	3	99	
Sit met effe hulp	1	2	3	99	
Loop alleen	1	2	3	99	
Loop met leiding	1	2	3	99	
Loop agteruit	1	2	3	99	
Fyn Motories					
Gooi artikels	1	2	3	99	
Ryk na en tel artikels op	1	2	3	99	
Volg bewegende speelgoed horisontaal	1	2	3	99	
Speel met rollende bal	1	2	3	99	
Wys met voorvinger	1	2	3	99	
Gooi bal na persoon	1	2	3	99	
Persoonlike Ontwikkeling					
Glimlag	1	2	3	99	
Waai totsiens	1	2	3	99	
Toon twee of meer kenbare emosies	1	2	3	99	
Plesier, bangheid, ongelukkigheid, ontsteldnes, kwaadheid					
Volg eenvoudige aanvraag "gee my die koppie".	1	2	3	99	
Finger voed (duim en voorvinger) WYS	1	2	3	99	
Ken dele van liggaam	1	2	3	99	
Hande, hare, voete, oe, neus, mond					

Tale					
Skud kop vir NEE	1	2	3	99	
Maak twee verskillende geluide	1	2	3	99	
Noem artikels (2)	1	2	3	99	
Luister na geselskap	1	2	3	99	
Identifiseer artikels (3)	1	2	3	99	
Een word (mama, papa) definitief en menigsvol	1	2	3	99	
Performance:					
Hand na mond	1	2	3	99	
Beweeg speelding van hand tot hand	1	2	3	99	
Vat speelding in hand en hou	1	2	3	99	
Sit twee blokkies in 'n doos en sit deksel op WYS	1	2	3	99	
3-gat plank (3 in) WYS	1	2	3	99	
Vind speelding onder koppie	1	2	3	99	
Vroe kinder jare	**3-4 yr**	**4-5yr**	**5-6yr**		
Growwe motories					
Kan op een voet hop (3 hoppe)	1	2	3	99	
Statiese balans: kan op een been staan vir 3 sek +	1	2	3	99	
Kan op lyn loop vir tenminste 1.2m	1	2	3	99	
Klim trappe: een voet op elke trap soos volwassene	1	2	3	99	
Kan tennis bal hop en vang	1	2	3	99	
Kan hardloop en medium groote bal skop	1	2	3	99	
Fyn motories					
Bou toring van 8+ stenne WYS	1	2	3	99	
Teken persoon	1	2	3	99	
Kopier 'n sirkel	1	2	3	99	
Kopier 6+ letters	1	2	3	99	
Kan vierkant in twee ewergroot dele sny (WYS)	1	2	3	99	
Kan op lyn sny WYS	1	2	3	99	
Persoonlikke ontwikkeling					
Gee eerste naam	1	2	3	99	
Ken ouderdom	1	2	3	99	
Kan self aan- en uittrek	1	2	3	99	
Ken geslag	1	2	3	99	
Was eie hande en gesig met hulp	1	2	3	99	
Kan artikel gaan haal in winkel op aanvraag	1	2	3	99	
Taal					
Kan 12 artikels in doos noem WYS	1	2	3	99	
Ken teeenoorgesteldes	1	2	3	99	
Herhaal 'n 6 sillabel sin	1	2	3	99	
Ek het 'n klein katjie					
Noem 6 kleure	1	2	3	99	
Defineer deur gebruik (2+)	1	2	3	99	
Herhaal een 10 sillabel sin	1	2	3	99	
My hond is 'n baie gooie vriend vir my					
Performance: SHOW ALL					
Trein suksessvol onder brug	1	2	3	99	
Sit nege blokkie in doos in onder 50sekondes	1	2	3	99	
Bou 'n brug met 3 dose	1	2	3	99	
Versaamel blokkies volgens kleur	1	2	3	99	

Herbou geskroewe speelding	1	2	3	99	
Patroonmaak 5 (50 secs)	1	2	3	99	
Praktiese redeneering					
Vergelyk 2 insette vir grotte	1	2	3	99	
Tel 4 bakstenne korrek	1	2	3	99	
Weet hoevelheid vingers op elke hand	1	2	3	99	
Vergelyk twee torings vir grotte	1	2	3	99	
Ken wat kos meer?	1	2	3	99	
n Fiets of 'n bal?					
Vergelyk twee streepe vir lengte	1	2	3	99	

INTERNAL AUDIT QUESTIONS (Confidence rating)

1. This woman's misrepresentation? ..... ☐☐

   1 = Yes 2 = No 88 = Unknown

   The following factors considered in choosing how to answer this question:

   a. Contradictory information in child's chart (e.g. documentation of intoxication at birth)
   b. Contradictory information from reliable source
   c. Contradictory response to questions within the interview
   d. Subjective assessment of the interviewer based on interaction with and observation of the woman during the interview (body language, etc.)

2. This woman's inability to understand?..... ☐☐

   1 = Yes 2 = No 88 = Unknown

   The following factors are considered in choosing how to answer this question:

   a. Language
   b. Intellectual ability
   c. Psychaitric disorders
   d. Contradictory response to questions within the interview

3. What was the primary source of "risk" in this woman's life (at the time of the pregnancy of interest)?
   (circle ALL that apply)

   1 = Woman used alcohol
   2 = Excessive family involvement in alcohol
   3 = Partner used alcohol
   4 = Friends used alcohol
   5 = Woman used other drugs
   6 = Other psychiatric diagnosis
   7 = Other (specify) _____

4. Risk category of this woman TODAY for producing future affected child?..... ☐☐

   1 = High risk 3 = Low risk
   2 = Medium risk 4 = Lowest risk
   88 = Unknown

The following factors are considered in choosing how to answer this question:

a. High risk
   1) The woman is currently drinking and pregnant
   2) The woman is currently drinking and is not using any form of birth control
   3) The woman is currently using other drugs
b. Medium risk

1) The woman has been abstinent < 1 year, and is not using any form of birth control
2) The woman has been abstinent < 1 year; however, her partner is still drinking and/or the woman has not made any positive changes in her social situation.
3) The woman drank only before her pregnancy was diagnosed; was abstinent for remainder of pregnancy
4) The woman has been abstinent < 1 year, and the woman's partner has had a vasectomy.

c. Low risk
1) The woman has been abstinent > 1 year; currently she does not have a partner who is drinking or has no partner
2) The woman has been abstinent > 1 year, and she has made positive changes in her social situation.
3) The woman is using semi-permanent method of birth control (depo-provera, norplant)
4) The woman has been abstinent > 1 year, and the woman 's partner has had a vasectomy
5) The woman is currently pregnant, and there is no information to suggest any use so far in pregnancy.

d. Lowest risk
1) The woman has had surgical sterilization (i.e., tubal ligation, or hysterectomy

APPENDIX D: Histogram Distributions for GMDS Infant Version Subscales at 7-12months (TIME 1) for FAS/PFAS Group

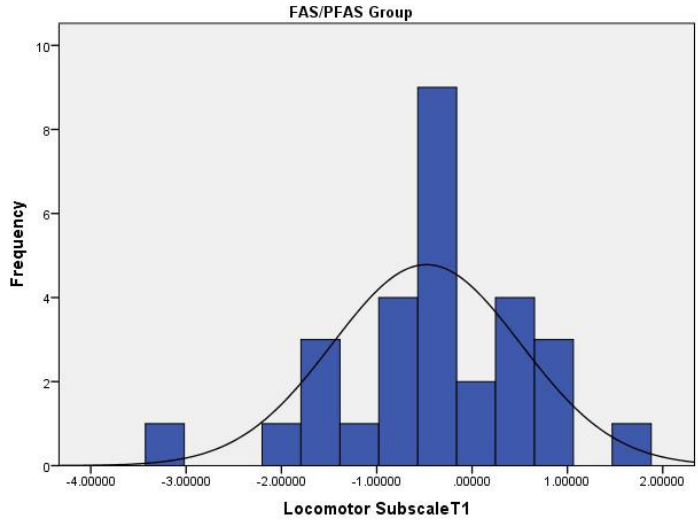


Figure 6. Histogram of Locomotor subscale at Time 1

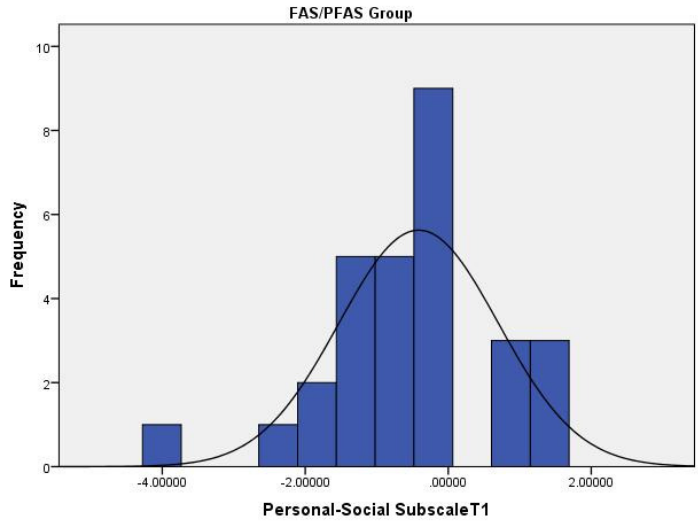


Figure 7. Histogram of Personal-Social subscale at Time 1

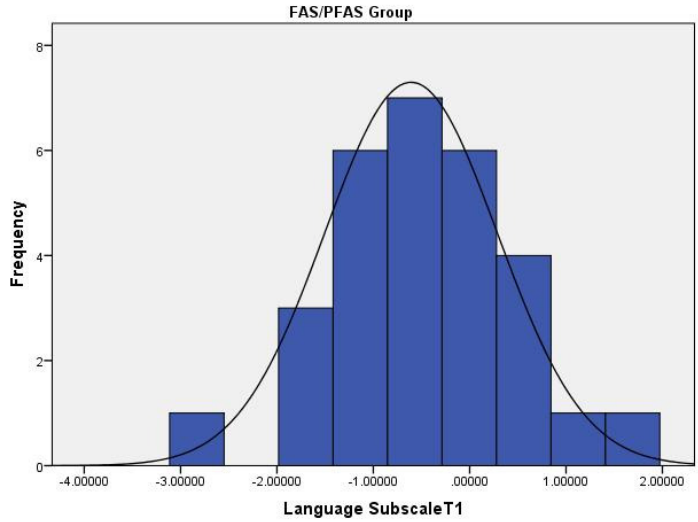


Figure 8. Histogram of Language subscale at Time 1

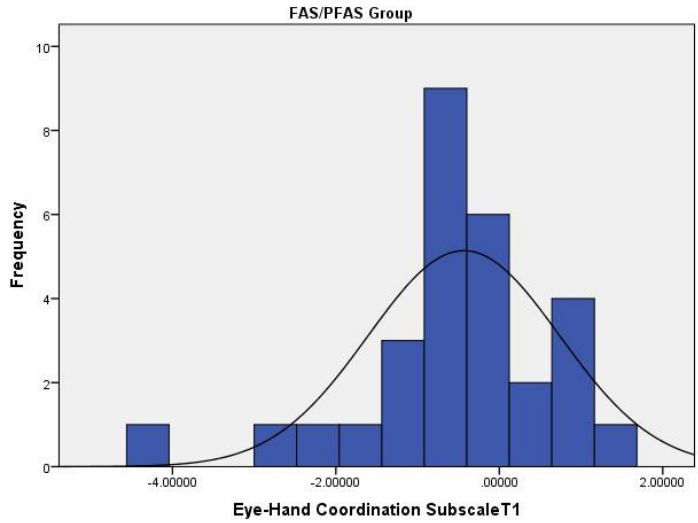


Figure 9. Histogram of Eye-Hand Coordination subscale at Time 1

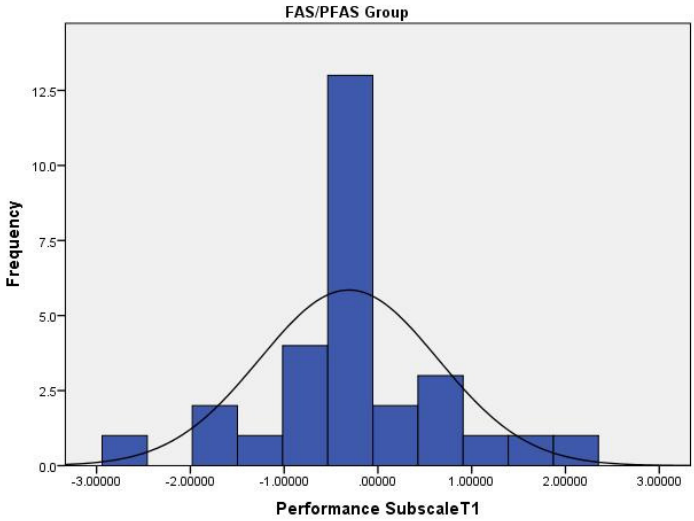


*Figure 10***.** Histogram of Performance subscale at Time 1

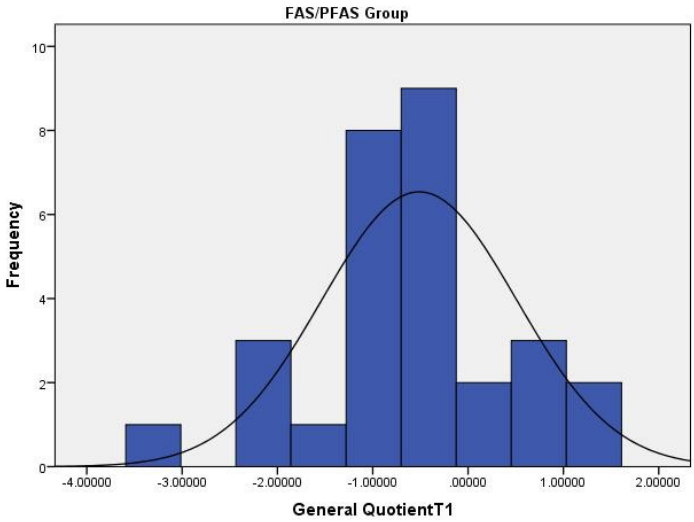


Figure 11. Histogram of General Quotient at Time 1

APPENDIX E: Histogram Distributions for GMDS Infant Version Subscales at 7-12months (TIME 1) for PAE Group

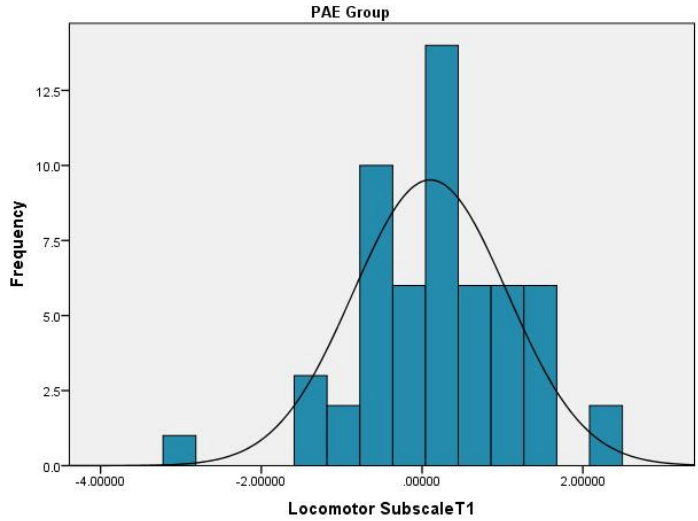


Figure 12. Histogram of Locomotor subscale at Time 1

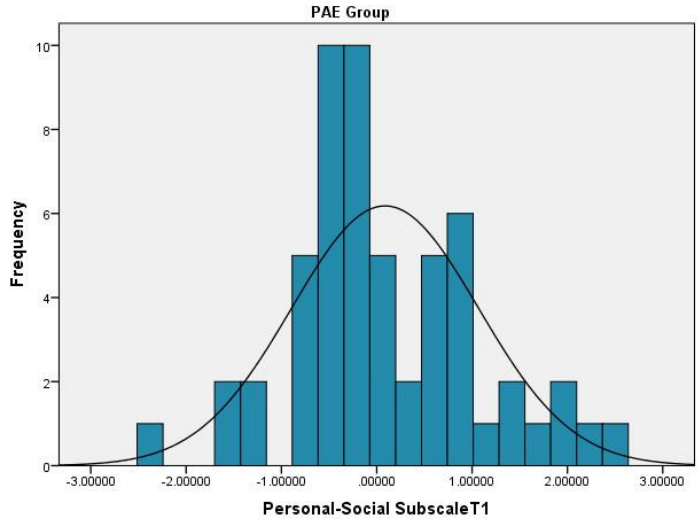


Figure 13. Histogram of Personal-Social subscale at Time 1

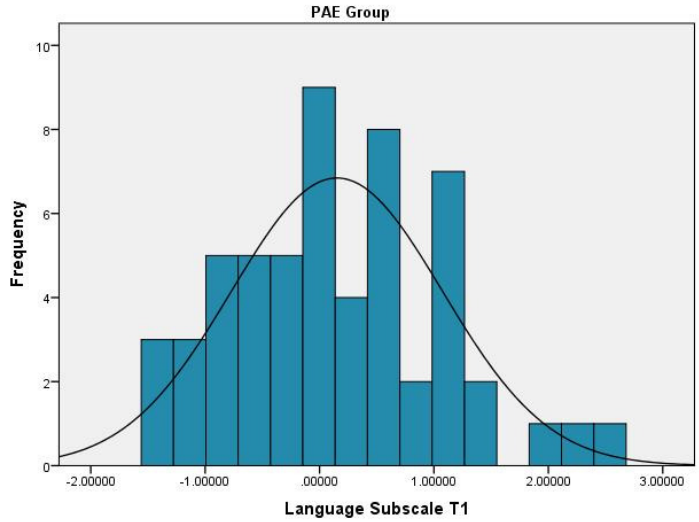


Figure 14. Histogram of Language subscale at Time 1

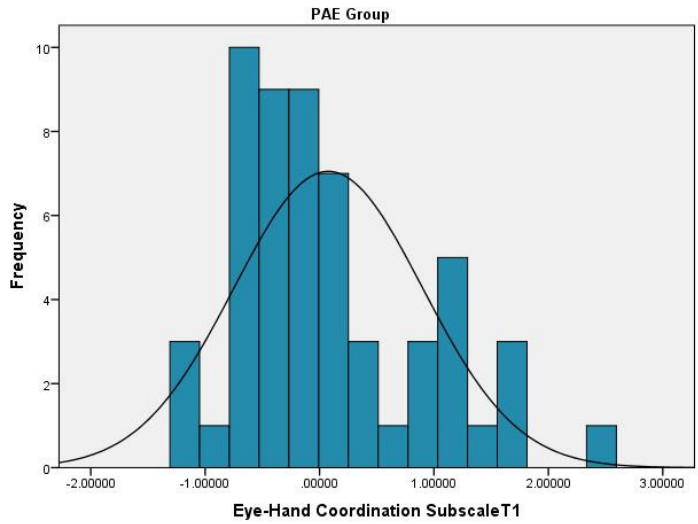


Figure 15. Histogram of Eye-Hand Coordination subscale at Time 1

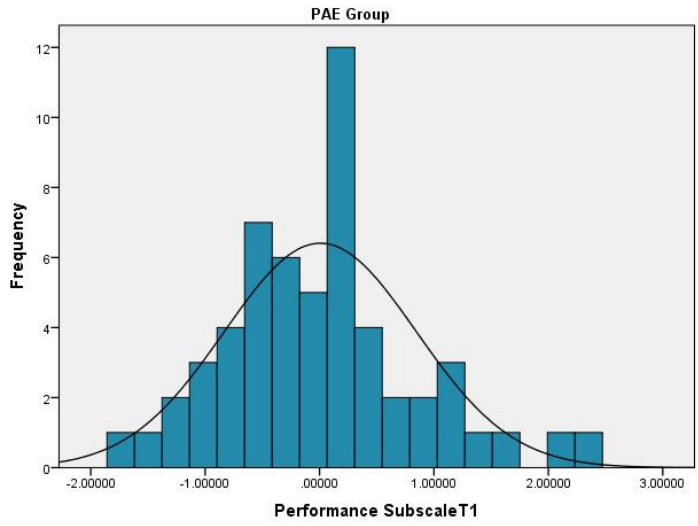


Figure 16. Histogram of Performance subscale at Time 1

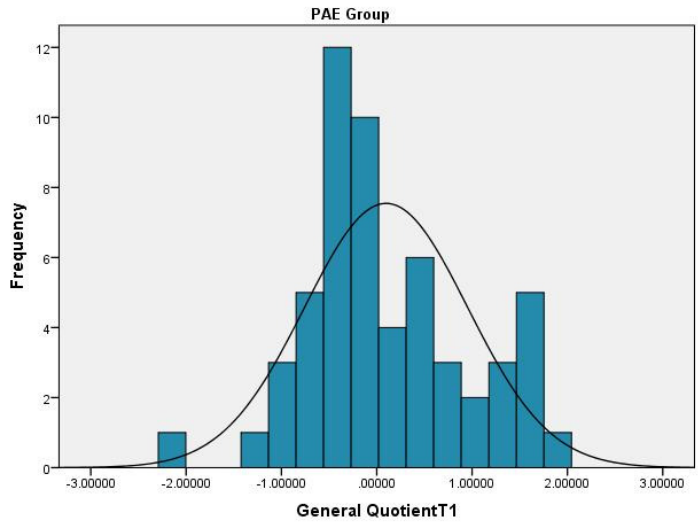


Figure 17. Histogram of General Quotient at Time 1

APPENDIX F: Histogram Distributions for GMDS Infant Version Subscales at 7-12months (TIME 1) for Control Group

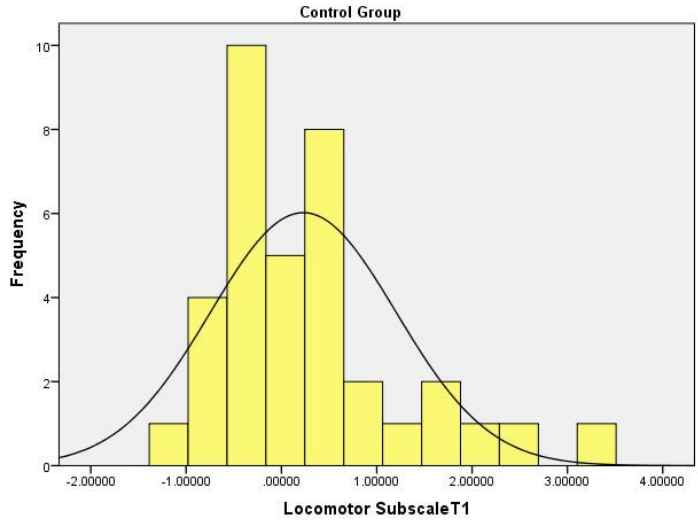


Figure 18. Histogram of Locomotor subscale at Time 1

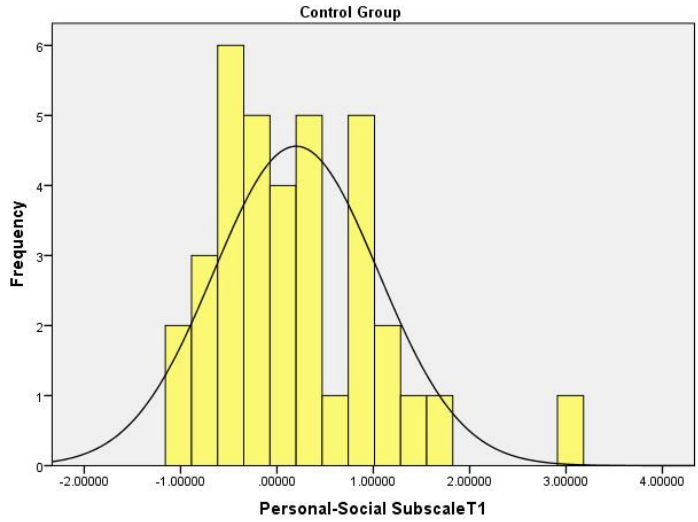


Figure 19. Histogram of Personal-Social subscale at Time 1

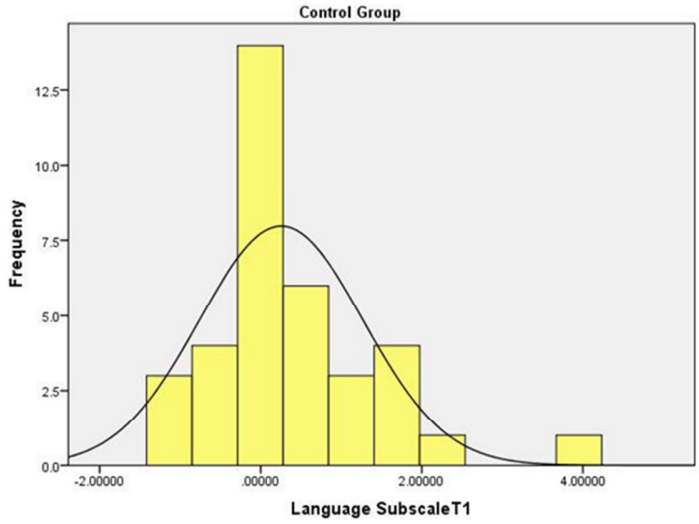


Figure 20. Histogram of Language subscale at Time 1

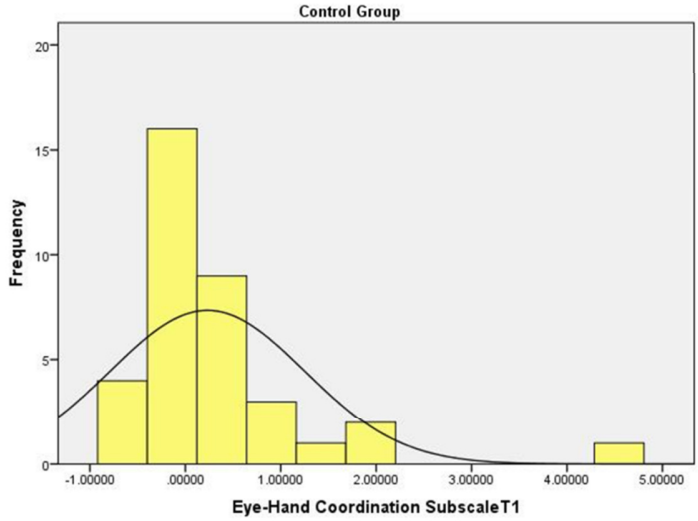


Figure 21. Histogram of Eye-Hand Coordination subscale at Time 1

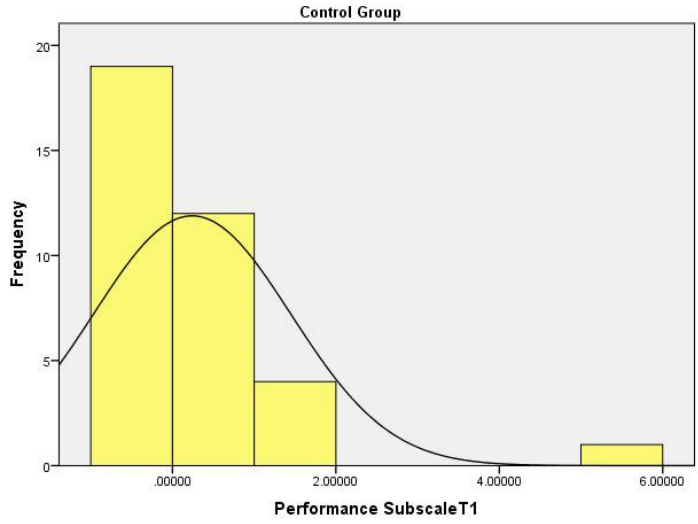


Figure 22. Histogram of Performance subscale at Time 1

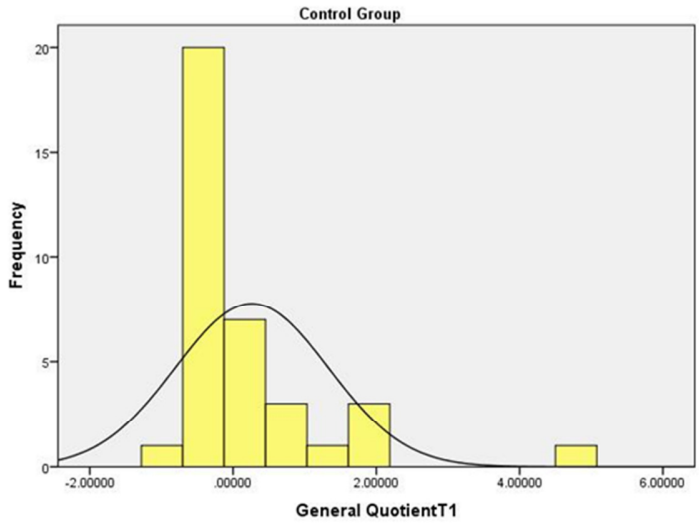


Figure 23. Histogram of General Quotient at Time 1

APPENDIX G: Histogram Distributions for GMDS/ER Version Subscales at 5 years (TIME 2) for FAS/PFAS Group

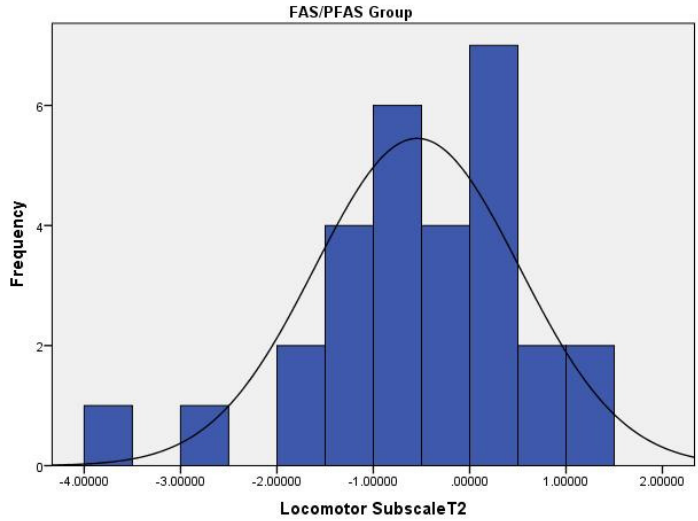


Figure 24. Histogram of Locomotor subscale at Time 2

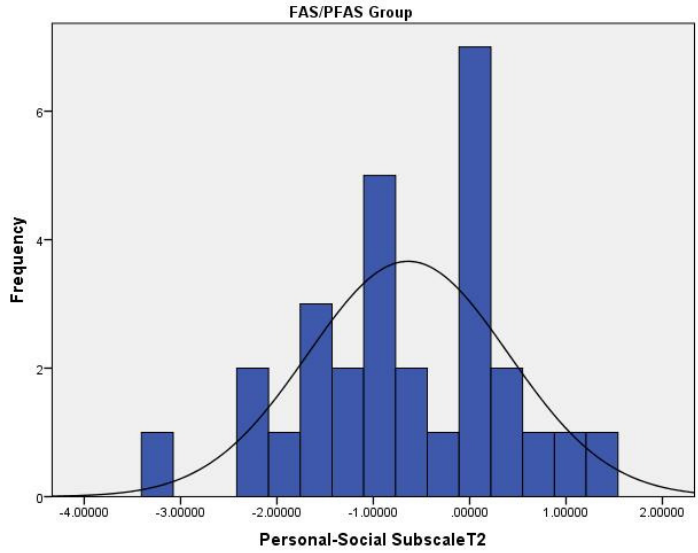


Figure 25. Histogram of Personal-Social subscale at Time 2

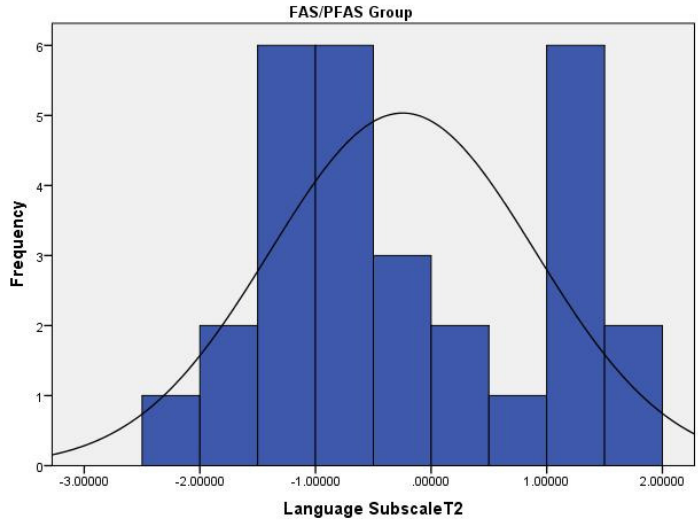


Figure 26. Histogram of Language subscale at Time 2

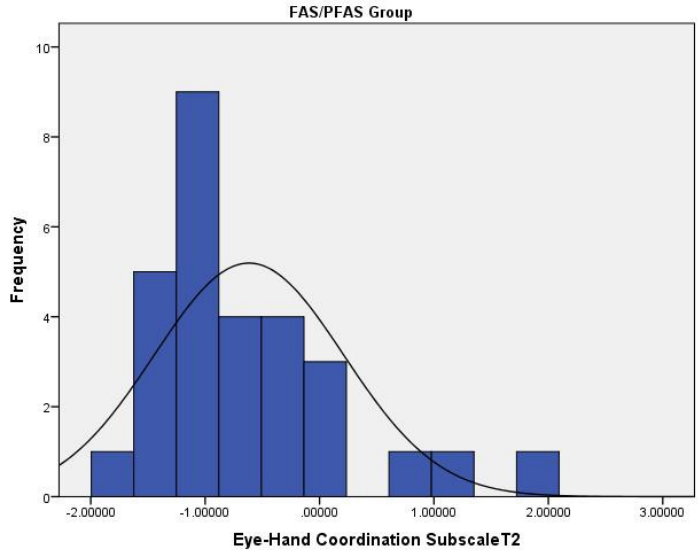


Figure 27. Histogram of Eye-Hand Coordination subscale at Time 2

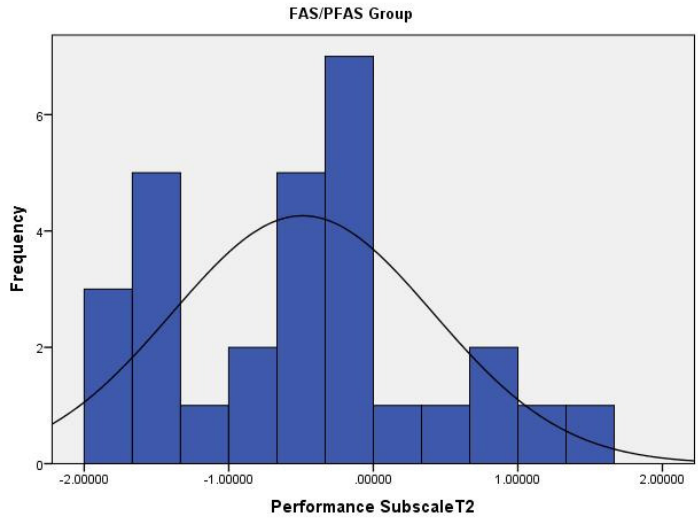


Figure 28. Histogram of Performance subscale at Time 2

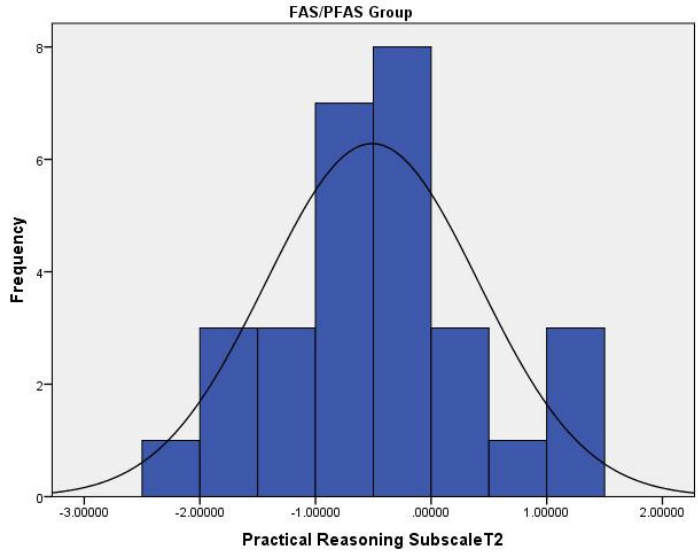


Figure 29. Histogram of Practical Reasoning subscale at Time 2

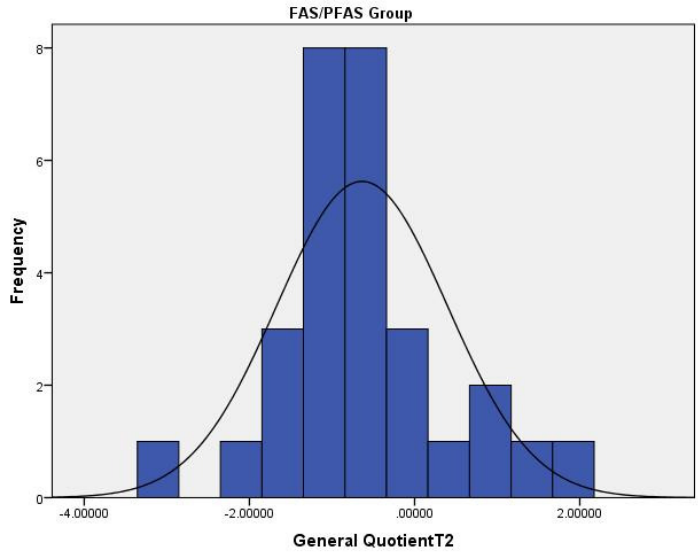


Figure 30. Histogram of General Quotient at Time 2

APPENDIX H: Histogram Distributions for GMDS/ER Version Subscales at 5 years (TIME 2) for PAE Group

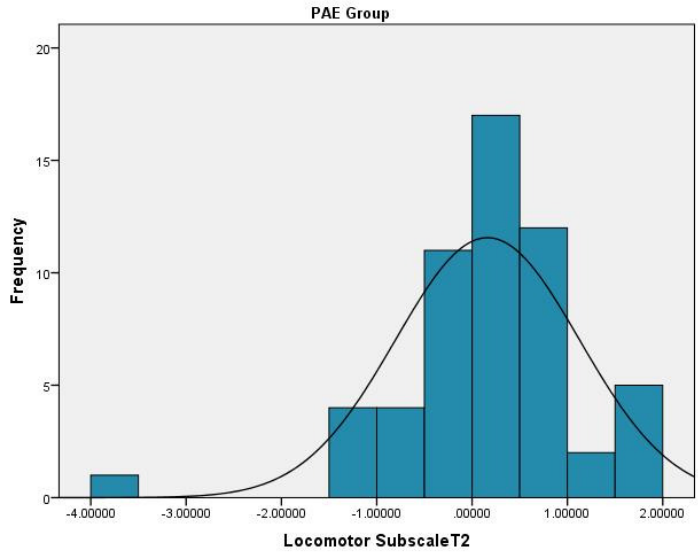


Figure 31. Histogram of Locomotor subscale at Time 2

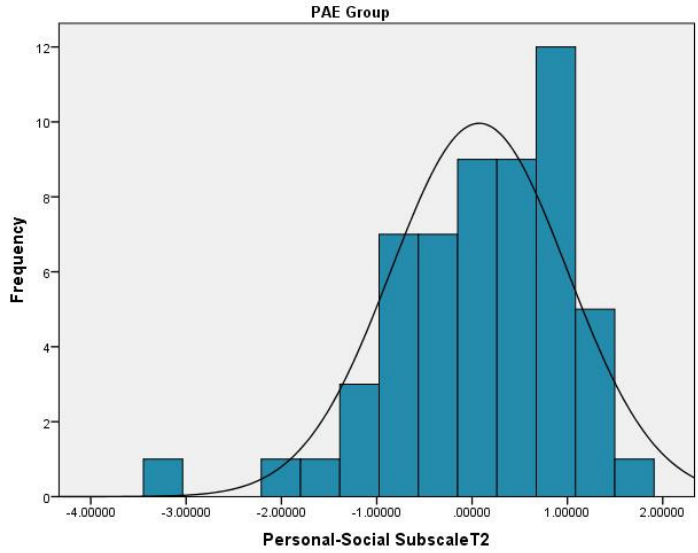


Figure 32. Histogram of Personal-Social subscale at Time 2

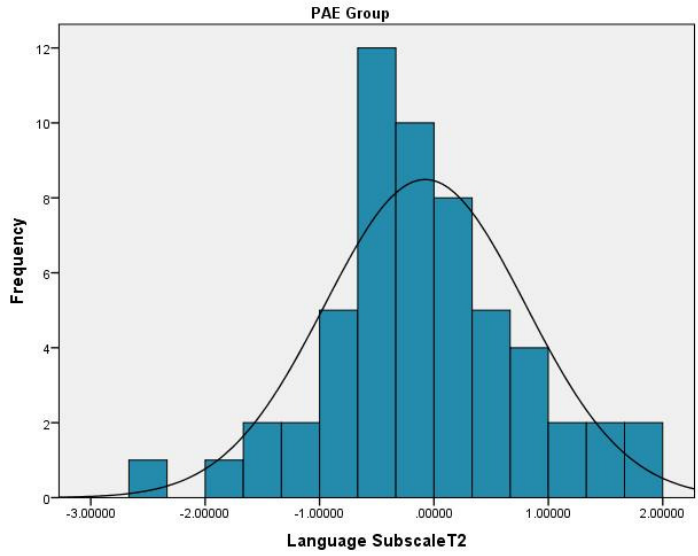


Figure 33. Histogram of Language subscale at Time 2

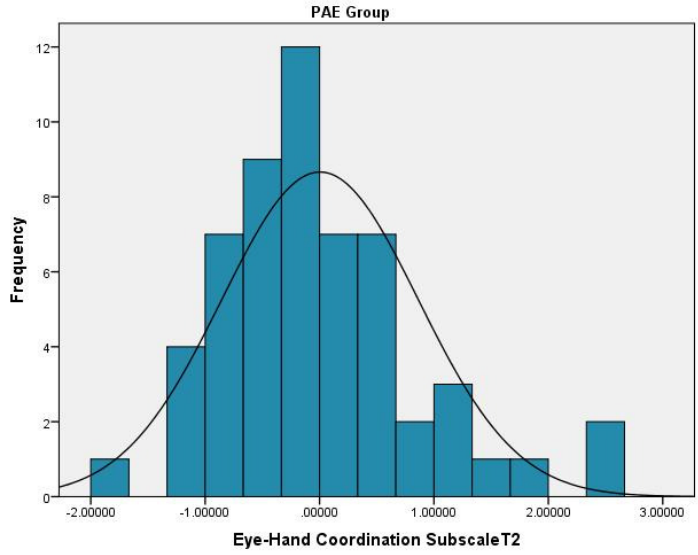


Figure 34. Histogram of Eye-Hand Coordination subscale at Time 2

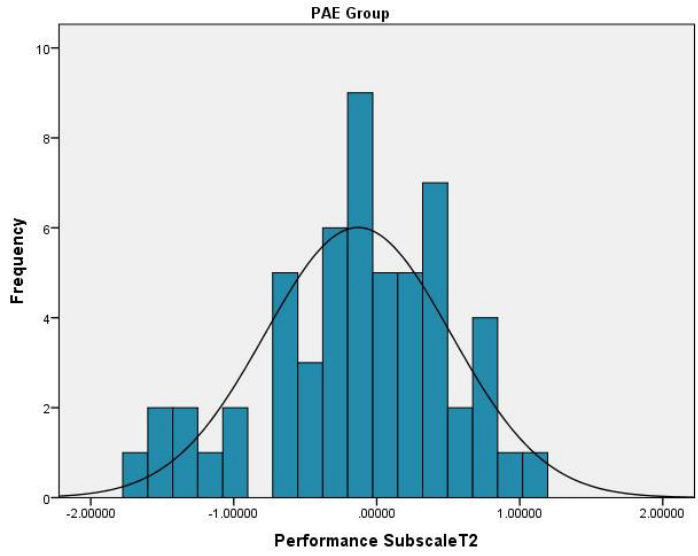


Figure 35. Histogram of Performance subscale at Time 2

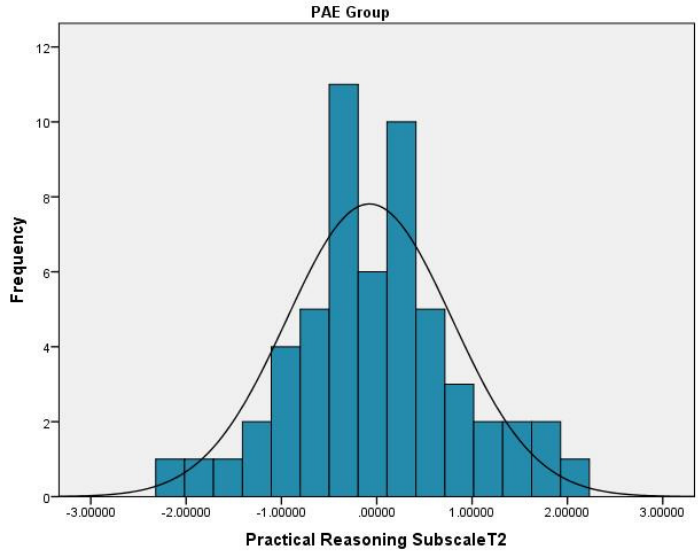


Figure 36. Histogram of Practical Reasoning subscale at Time 2

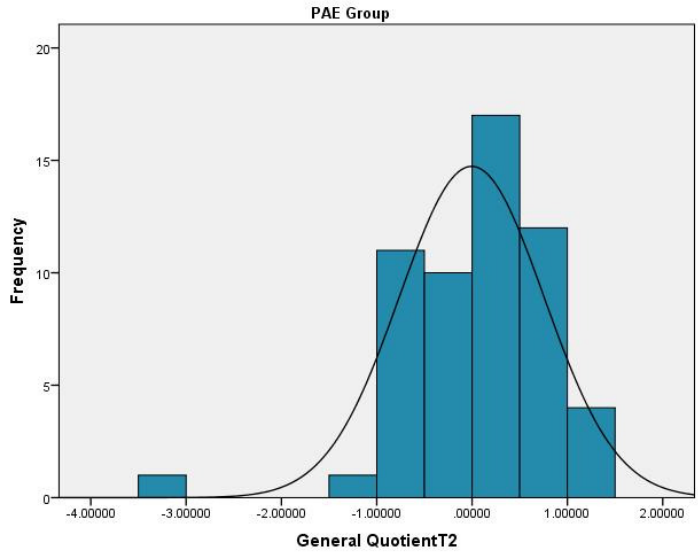


Figure 37. Histogram of General Quotient at Time 2

APPENDIX I: Histogram Distributions for GMDS/ER Version Subscales at 5 years (TIME 2) for Control Group

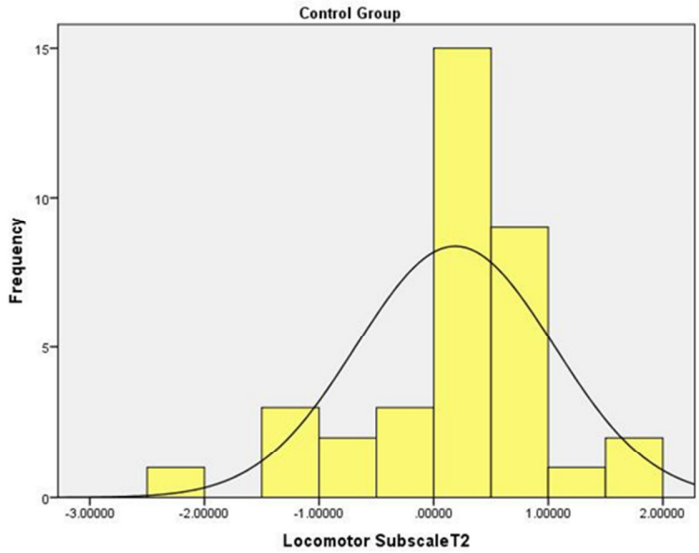


Figure 38. Histogram of Locomotor subscale at Time 2

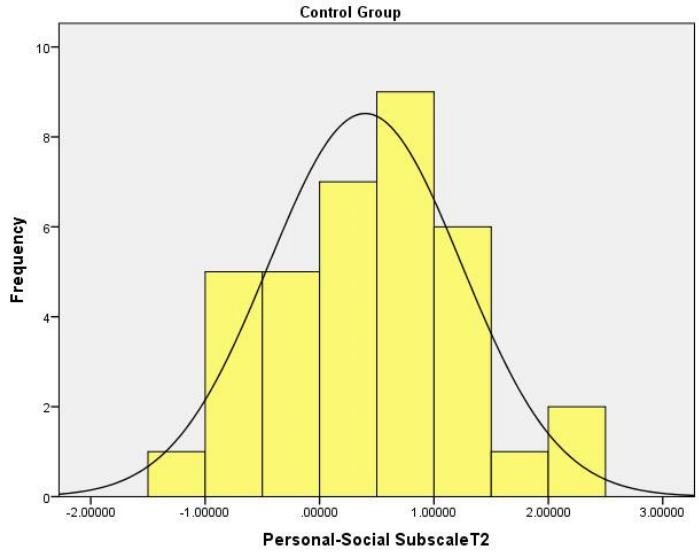


Figure 39. Histogram of Personal-Social subscale at Time 2

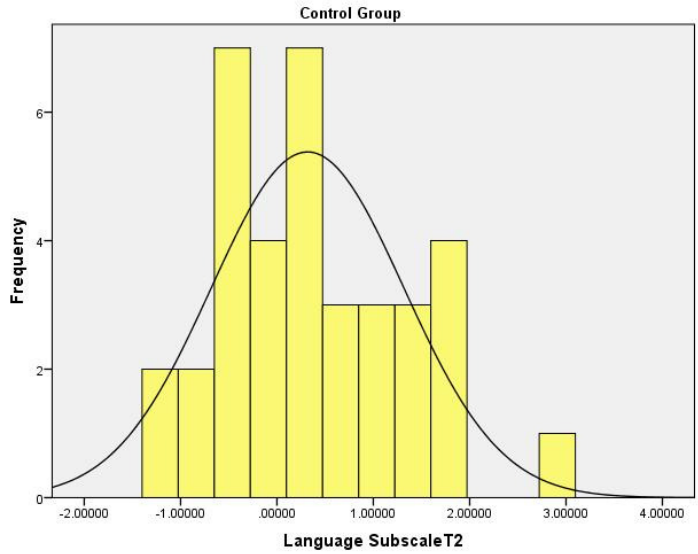


Figure 40. Histogram of Language subscale at Time 2

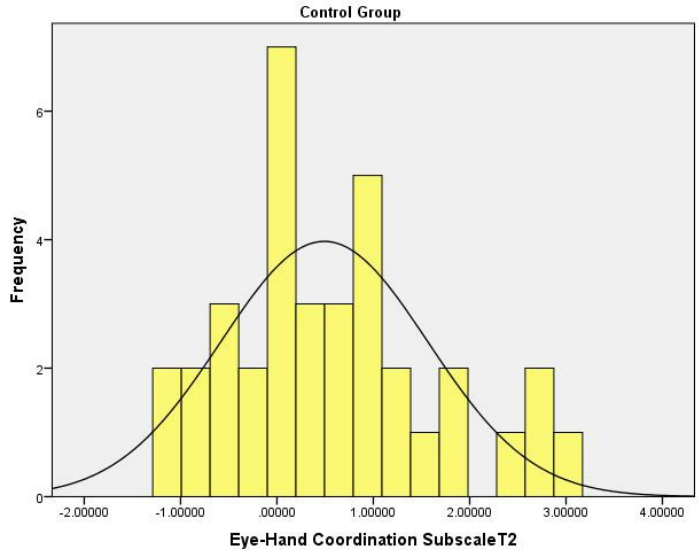


Figure 41. Histogram of Eye-Hand Coordination subscale at Time 2

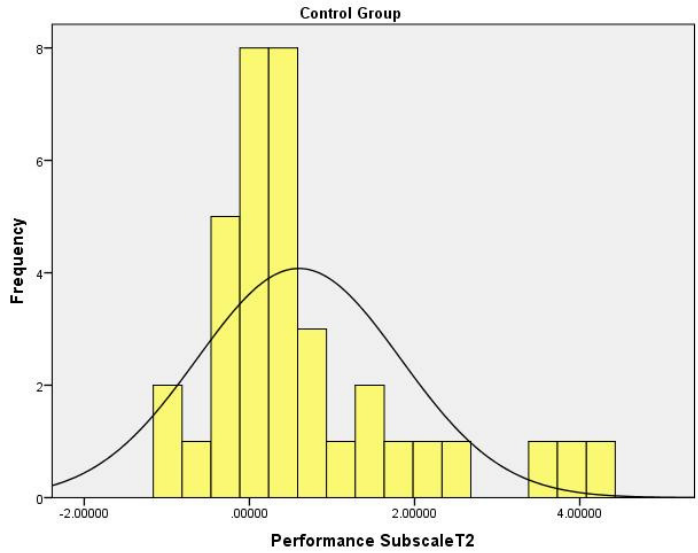


Figure 42. Histogram of Performance subscale at Time 2

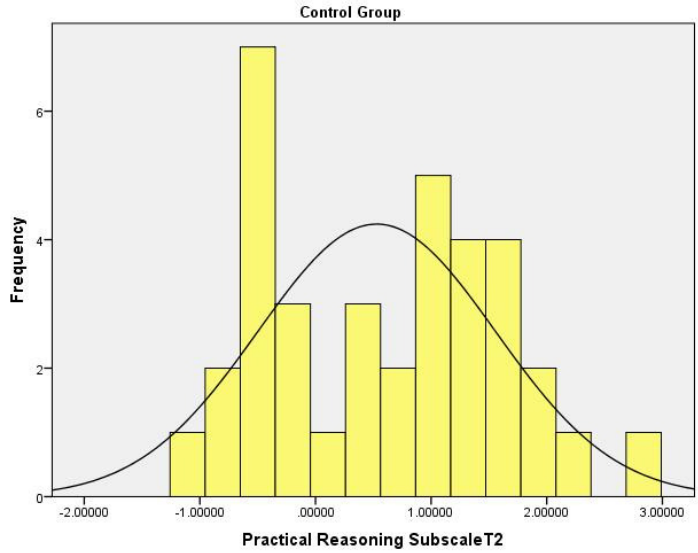


Figure 43. Histogram of Practical Reasoning subscale at Time 2

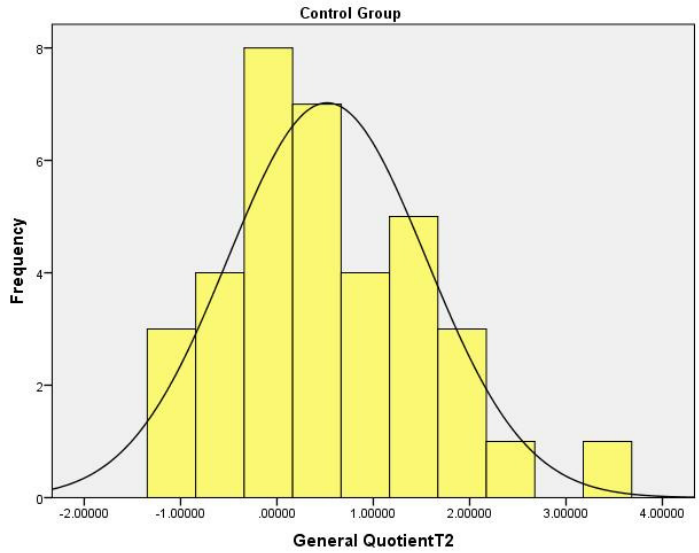


Figure 44. Histogram of General Quotient at Time 2