

https://dspace.org/

A cost analysis of the conventional culture method versus polymerase chain reaction testing for methicillin-resistant staphylococcus aureus at a South African public hospital

Ahmed-Hassen, Sadiyya

2016-10-12
http://hdl.handle.net/10539/21180

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

A COST ANALYSIS OF THE CONVENTIONAL CULTURE METHOD VERSUS POLYMERASE CHAIN REACTION TESTING FOR METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* AT A SOUTH AFRICAN PUBLIC HOSPITAL

Sadiyya Ahmed-Hassen



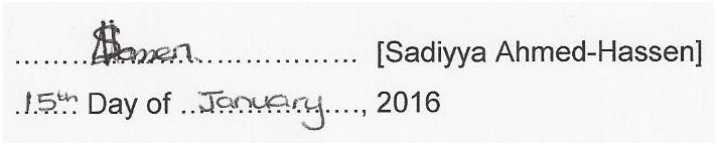
A Dissertation Submitted to the Faculty of Health Sciences,
University of the Witwatersrand, Johannesburg,
in fulfilment of the requirements for the degree of
Master of Science in Medicine
in the Department of Pharmacy and Pharmacology

The financial assistance of the National Research Foundation (NRF) towards this research is hereby acknowledged. Opinions expressed and conclusions arrived at, are those of the author and are not necessarily to be attributed to the NRF.

Johannesburg, January 2016

DECLARATION

I, Sadiyya Ahmed-Hassen, declare that this dissertation is my own work. It is being submitted for the degree of Master of Science in Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.



ABSTRACT

Methicillin-Resistant *Staphylococcus aureus* (MRSA) infections increase the cost and consequences of patient care within hospitals. Patients can be tested for MRSA using the Conventional Culture Method or new rapid Polymerase Chain Reaction (PCR) tests, such as the Xpert MRSA test. International studies have compared the costs and consequent management pathways for these two methods of MRSA testing. However, in the South African context where socio-economic status and access to healthcare may contribute different influences, no such models exist. Therefore, the aim of this study was to investigate the costs of the management pathways associated with using the current Conventional Culture Method for MRSA testing, to construct decision-tree-analytic models and compare them to the new PCR testing, in order to inform decision-making.

TreeAge decision-tree-analytic models were developed to depict the current pathways, and associated costs, incurred by patients with a suspected MRSA infection in an orthopaedic and vascular ward at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) in South Africa in 2013. These models were then compared to theoretical pathways including implementing the Xpert MRSA. The models were populated with input parameters from observations conducted in the two wards, the microbiology laboratory and the main dispensary, and costs were calculated using the retrospective utilization reviews formulated from the antibiotics administered and laboratory tests that isolated MRSA in the study population. Sensitivity analyses were performed to evaluate the effect of the variables on the models.

The average total cost of antibiotics and MRSA laboratory tests utilised per patient in the orthopaedic and vascular wards were R3 846.82 and R2 964.39 respectively. Based on ethnographic observations and retrospective utilization reviews, three pathways for a patient with a suspected infection were identified: Empiric Antibiotics followed by Microscopy, Culture and Sensitivity (MCS); MCS followed by Empiric Antibiotics; Empiric Antibiotics and MCS concurrently. The fourth pathway included implementing the Xpert MRSA test. Analysis of these pathways revealed that implementation of the Xpert MRSA would be the optimal strategy in the orthopaedic ward, but the most expensive strategy in the vascular ward.

In conclusion, these costs and pathways highlight the utilization of scarce resources. Thus, it is suggested that, before new methods of MRSA testing are introduced, the current practices and pathways for patients with a suspected MRSA infection should be further evaluated and improved.

ACKNOWLEDGEMENTS

The completion of this study would not have been possible if it were not for certain individuals and organizations. Thus, not only are they acknowledged, but sincere appreciation is shown to:

My Supervisors, Dr Jacqui Miot and Mrs Shirra Moch, for their continuous guidance, expertise and encouragement.

The Department of Pharmacy and Pharmacology, Staff, Academic Interns and Master's Students for their motivation and understanding.

The CEO of CMJAH, Ms Bogoshi, for the permission granted to conduct this study at CMJAH. The Head of the Orthopaedic and Vascular wards, Professor Mkhululi Lukhele and Professor Martin Veller, for allowing the study to be conducted in their wards as well as their clinical team and consultants for their assistance. The Head of the Hospital's Medical Records Room for consent to access and document the required retrospective patient records. The pharmacist at the main dispensary at CMJAH for her contribution of information concerning dispensing of antibiotics. Dr Norma Bosman from the National Health Laboratory Service (NHLS) Microbiology Laboratory for her input and advice. Dr Lumbwe Chola for reviewing the decision-tree-analytic models.

The NHLS Information Systems for the provision of requested information regarding MRSA testing and costing information at CMJAH in 2013.

Financial assistance of the National Research Foundation Scarce Skills Master's Scholarship 2014 and the National Research Foundation Extension Master's Scholarship 2015. The University of the Witwatersrand, Johannesburg, Research Office, Faculty of Health Sciences, Faculty Research Committee Individual Research Grant 2013 and Staff Bursary 2013 – 2015.

Last but not least, my Family for their love, support and patience.

And my Success can only come from Allah. In Him I Trust, and unto Him I Look.

RESEARCH OUTPUTS

Conference Presentations

Ahmed-Hassen S, Moch S, Miot J. Building a Decision-Tree-Analysis Model as a Tool for Cost Comparison of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) Management in The Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).
Poster Presentation at the 17th World Congress of Basic and Clinical Pharmacology (WCP2014), 13-18 July 2014, held at the Cape Town International Convention Centre (CTICC), Cape Town.
3rd Prize Poster Award in Clinical Pharmacology from the South African Society for Basic and Clinical Pharmacology.

Ahmed-Hassen S, Miot J, Moch S. Building a Decision-Tree-Analysis Model as a tool for cost comparison of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) management in Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).
Poster Presentation at the University of the Witwatersrand, Faculty of Health Sciences Biannual Research Day, 17 September 2014, held at the University of the Witwatersrand, Faculty of Health Sciences, Johannesburg.

Ahmed-Hassen S, Miot J, Moch S. Building a Decision-Tree-Analysis Model as a Tool for Cost Comparison of MRSA Management in CMJAH.
Oral Presentation at the University of the Witwatersrand, 6th Cross-Faculty Graduate Symposium, 28-29 October 2014, held at the University of the Witwatersrand, Johannesburg.

Ahmed-Hassen S, Miot J, Moch S. Cost of Diagnostic Options and Consequent Treatment Pathways for Methicillin Resistant *Staphylococcus Aureus*: A Decision-Tree Analysis.
Oral Presentation at the South African Society for Basic & Clinical Pharmacology and the Toxicological Society of South Africa Congress, hosted by the WITS Pharmacology Division, Monday 31 August - 2 September 2015, held at the WITS Club, Johannesburg.

Conference Published Abstracts

Ahmed-Hassen S, Moch S, Miot J. (2014). Building a Decision-Tree-Analysis Model as a Tool for Cost Comparison of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) Management in The Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). *Basic Clin Pharmacol Toxicol* **115**(Suppl. 1): 61

Ahmed-Hassen S, Miot J, Moch S. (2015). Building a Decision-Tree-Analysis Model as a tool for cost comparison of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) management in Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). *South Afr J Infect Dis:* **30**(1): 54-55

TABLE OF CONTENTS

Declaration ..... **ii**

Abstract ..... **iii**

Acknowledgements ..... **iv**

Research Outputs ..... **v**

Table of Contents ..... **vii**

List of Tables ..... **xv**

List of Figures ..... **xviii**

Abbreviations ..... **xxi**

1. INTRODUCTION **1**

1.1 Background to Research **1**

1.2 Aim **3**

1.3 Objectives **3**

2. LITERATURE REVIEW **4**

2.1 Hospital-Acquired Infections **4**

2.1.1 Overview of Hospital-Acquired Infections 4

2.1.2 Types of Hospital-Acquired Infections 4

2.1.3 Factors that Promote Infection in Hospitalised Patients 5

2.1.4 Impact of Hospital-Acquired Infections 5

2.2 Methicillin-Resistant *Staphylococcus aureus* **6**

2.2.1 Overview of MRSA 6

2.2.2 Prevalence of MRSA 6

2.2.3 Clinical Manifestation of MRSA 8

2.2.4 Transmission and Colonization of MRSA 9

2.3 Preventing and Managing MRSA **9**

2.3.1 Infection Control 9

2.3.2 Infection Control in South Africa 11

2.3.3 Antibiotic Treatment Pathways 11

2.4 Laboratory Tests for MRSA **13**

2.4.1 Screening versus Diagnostic 13

2.4.2 Conventional Culture Method 13
2.4.3 PCR Testing Method 14
2.5 Ethnography in Healthcare 16
2.6 South African Healthcare System 16
2.6.1 Private Sector versus the Public Sector 16
2.6.2 Costing System used in the Public Healthcare System 17
2.7 Economic Evaluations of Healthcare Programmes 18
2.7.1 Economic Evaluations 18
2.7.2 Cost-Analysis 19
2.7.3 Decision-Analytic Modelling 20
2.7.4 Economic Evaluations In the South African Healthcare Context 21
2.8 Building Decision-Tree-Analytic Models to Compare the Conventional Culture Method and PCR Testing for MRSA 22
3. METHODOLOGY 24
3.1 Theoretical Framework 24
3.2 Study Design 24
3.3 Study Site 25
3.4 Study Population 25
3.5 Study Duration 27
3.6 Ethical Considerations 28
3.7 Data Collection Procedures 28
3.7.1 Ethnographic Observations 28
3.7.1.1 Data Collection by Ethnographic Observations 29
3.7.1.1.1 Clinical Ward Observations 29
3.7.1.1.2 NHLS Microbiology Laboratory Observations 30
3.7.1.1.3 Antibiotic Dispensary Observations 31
3.7.2 Retrospective Records and Antibiotic Utilization Review 31
3.7.2.1 Data Extraction Procedure 31
3.7.2.2 Collection of Retrospective Patient Data 32
3.7.3 Cost Analysis 33

3.7.3.1 Costing Information 33
3.7.3.1.1 Antibiotic Costing Information 33
3.7.3.1.2 NHLS Laboratory Test Costing Information 33
3.7.3.1.3 Xpert MRSA Costing information 34
3.7.4 Decision-Tree-Analytic Models 34
3.7.4.1 Patient Management Pathways 34
3.7.4.2 Decision-Tree-Analytic Model Structure 35
3.7.4.2.1 Decision-Tree-Analytic Model Structure for the Orthopaedic Ward 35
3.7.4.2.2 Decision-Tree-Analytic Model Structure for the Vascular Ward 38
3.7.4.3 Decision-Tree-Analytic Model Parameters 41
3.7.4.3.1 Variables 41
3.7.4.3.2 Probabilities 42
3.7.4.3.3 Payoffs 43
3.8 Data Analysis 43
3.8.1 Analysis of Ethnographic Observations 43
3.8.2 Analysis of Retrospective Records and Antibiotic Utilization Review 43
3.8.2.1 Retrospective Patient Data Analysis 43
3.8.2.1.1 Antibiotic Utilization Review 44
3.8.2.1.2 Microbiology Laboratory Test Data Review 44
3.8.3 Cost Analysis Cost Calculations 45
3.8.3.1 Antibiotic Cost Calculations 45
3.8.3.2 NHLS Laboratory Test Cost Calculations 46
3.8.3.3 Antibiotic Utilization plus NHLS Laboratory Tests Cost Calculations 47
3.8.4 Analysis of the Decision-Tree-Analytic Models 47
3.8.4.1 Rollback and Rankings 47
3.8.4.2 Sensitivity Analysis 48
3.8.4.3 Tornado Analysis 48
4. RESULTS 49
4.1 Study Population 49
4.1.1 Patient Characteristics and Demographic Data 49

4.1.1.1 Orthopaedic Ward 49
4.1.1.2 Vascular Ward 50
4.2 Ethnographic Observations 51
4.2.1 Clinical Ward Observations 51
4.2.1.1 Ward Rounds 52
4.2.1.2 Patient Notes 52
4.2.1.3 Infection Control 52
4.2.1.4 Septic Workup 53
4.2.1.5 Isolation 54
4.2.1.6 Antibiotic Administration 54
4.2.2 NHLS Microbiology Laboratory Observations 55
4.2.2.1 Conventional Culture Process 55
4.2.2.1.1 Planting 56
4.2.2.1.2 Microscopy 56
4.2.2.1.3 Culture 57
4.2.2.1.4 Picking 58
4.2.2.1.5 Antibiotic Sensitivity 58
4.2.2.2 Timing Involved in the Conventional Culture Method 59
4.2.3 Antibiotic Dispensary Observations 60
4.2.3.1 Prescribing and Dispensing of Antibiotics 60
4.2.3.2 Restricted Use 61
4.2.3.3 Antibiotic Stewardship 62
4.2.4 Qualitative Analysis of Ethnographic Observation 62
4.2.4.1 Clinical Ward Observations 62
4.2.4.2 NHLS Microbiology Laboratory Observations 63
4.2.4.3 Antibiotic Dispensary Observations 64
4.3 Retrospective Records and Antibiotic Utilization Review 65
4.3.1 Antibiotic Utilization Review 65
4.3.1.1 Orthopaedic Ward 65
4.3.1.2 Vascular Ward 67

4.3.2 Microbiology Laboratory Test Data Review 71
4.3.2.1 Orthopaedic Ward 71
4.3.2.2 Vascular Ward 72
4.4 Cost Analysis 73
4.4.1 Antibiotic Cost Calculations 73
4.4.1.1 Orthopaedic Ward 73
4.4.1.2 Vascular Ward 74
4.4.2 NHLS Laboratory Test Cost Calculations 77
4.4.2.1 Orthopaedic Ward 77
4.4.2.2 Vascular Ward 78
4.4.3 Antibiotic Utilization plus NHLS Laboratory Tests Cost Calculation 79
4.4.3.1 Orthopaedic Ward 79
4.4.3.2 Vascular Ward 80
4.5 Decision-Tree-Analytic Models 83
4.5.1 Decision-Tree-Analytic Model Structure and Parameters 83
4.5.1.1 Variables 83
4.5.1.2 Complete Decision-Tree-Analytic Models 86
4.5.2 Analysis of the Decision-Tree-Analytic Models 91
4.5.2.1 Rankings 91
4.5.2.2 Payoffs and Path Probabilities 91
4.5.2.3 Sensitivity and Threshold Analysis 94
4.5.2.3.1 One-Way Sensitivity Analyses Performed for the Variables in the Decision-Tree-Analytic Models in the Orthopaedic Ward 95
4.5.2.3.2 One-Way Sensitivity Analyses Performed for the Variables in the Decision-Tree-Analytic Models in the Vascular Ward 99
4.5.2.4 Tornado Analysis 103
5. DISCUSSION 107
5.1 Overview of Research 107
5.2 Burden of MRSA 107
5.2.1 Burden of MRSA in South Africa 109
5.3 Study Population 110

5.3.1 Patient Characteristics and Demographic Data 111
5.4 Ethnographic Observations 112
5.4.1 Clinical Ward Observations 112
5.4.1.1 Ward Rounds 113
5.4.1.2 Infection Control Practices 114
5.4.1.3 Treatment of Patients 115
5.4.2 NHLS Microbiology Laboratory Observations 116
5.4.3 Antibiotic Dispensary Observations 118
5.5 Retrospective Records Review 120
5.5.1 Antibiotic Utilization Review 121
5.5.2 NHLS Microbiology Data Review 123
5.6 Cost Analysis 125
5.6.1 Antibiotic Cost Calculations 125
5.6.2 NHLS Laboratory Tests Cost Calculations 126
5.6.3 Cost Calculations of Antibiotic Utilization plus NHLS Laboratory Tests per Patient 127
5.7 Decision-Tree-Analytic Models 127
5.8 Limitations of the Study 129
5.8.1 Data Capturing 129
5.8.1.1 Patient Records 130
5.8.1.2 Medical Records Room 131
5.8.1.3 Main Dispensary 132
5.8.2 Protocols 132
5.8.3 Antibiotic Stewardship 133
5.8.4 Resources 133
5.8.5 Number of MRSA cases at CMJAH in 2013 133
5.9 Assumptions 134
6. CONCLUSION 135
7. RECOMMENDATIONS AND FUTURE RESEARCH 136
8. APPENDICES 138

Appendix 1 ..... **138**

8.1 Human Research Ethics Committee: Clearance Certificate **138**

Appendix 2 ..... **139**

8.2 Letter of Research Permission **139**

Appendix 3 ..... **140**

8.3 Data Collection Sheets **140**

8.3.1 Clinical Ward Observation Data Collection Sheet 140

8.3.2 Microbiology Laboratory Observation Data Collection Sheet 141

8.3.3 Antibiotic Dispensary Observation Data Collection Sheet 142

Appendix 4 ..... **143**

8.4 Individual Patient Case Report Form **143**

Appendix 5 ..... **144**

8.5 Costing Information **144**

8.5.1 Antibiotic Costing Information 144

8.5.2 NHLS Laboratory Test Costing Information 146

8.5.3 Xpert MRSA Costing Information 149

Appendix 6 ..... **150**

8.6 Codes and Categories Identified from the Ethnographic Observations **150**

8.6.1 Codes and Categories Identified from the Ethnographic Observations in the Clinical Wards 150

8.6.2 Codes and Categories Identified from the Ethnographic Observations in the NHLS Microbiology Laboratory 151

8.6.3 Codes and Categories Identified from the Ethnographic Observations in the Antibiotic Dispensary 153

Appendix 7 ..... **154**

8.7 Cost Calculations **154**

8.7.1 Antibiotic Cost Calculations 154

8.7.2 NHLS Laboratory Test Cost Calculation 159

8.7.3 Antibiotic Utilization plus NHLS Laboratory Tests Cost Calculation 163

Appendix 8 ..... **166**

8.8 Decision-Tree-Analytic Models in Rollback **166**

Appendix 9 ..... **170**

8.9 Threshold Analysis **170**

Appendix 10 ..... **172**

8.10 Plagiarism Report **172**

9. REFERENCES **173**

LIST OF TABLES

Table 1: Number of Microbiology Laboratory Tests and Number of Patients that Isolated MRSA per Ward at CMJAH in 2013.....26
Table 2: Age and Length of Stay in Hospital of the Patients in the Study Population in the Orthopaedic Ward in 2013 49
Table 3: Number of Patients with Common Diagnoses, Operations and Procedures Performed in the Study Population in the Orthopaedic Ward in 2013 50
Table 4: Age and Length of Stay in Hospital of the Patients in the Study Population in the Vascular Ward in 2013 51
Table 5: Number of Patients with Common Diagnoses, Operations and Procedures Performed in the Study Population in the Vascular Ward in 2013 51
Table 6: Hands-on Time and Incubation Time Involved in the Conventional Culture Method at the NHLS Microbiology Laboratory at CMJAH.....59
Table 7: Example of Restricted Dispensing of Certain Antibiotics at CMJAH.....61
Table 8: Summarised Codes and Categories Identified from the Ethnographic Observations in the Clinical Wards at CMJAH 62
Table 9: Summarised Codes and Categories Identified from the Ethnographic Observations in NHLS Microbiology Laboratory at CMJAH.....63
Table 10: Summarised Codes and Categories Identified from the Ethnographic Observations in Antibiotic Dispensary at CMJAH.....64
Table 11: Number of Antibiotics Administered per Patient and in Total in the Orthopaedic Ward in 2013.....65
Table 12: Number of Days of Administration, Number of Patients and Number of Prescriptions per Antibiotic in the Orthopaedic Ward in 2013.....66
Table 13: World Health Organization Defined Daily Dose (DDD) versus Prescribed Daily Dose (PDD) for Antibiotics in the Orthopaedic Ward in 2013 67
Table 14: Number of Antibiotics Administered per Patient and in Total in the Vascular Ward in 2013.....68
Table 15: Number of Days of Administration, Number of Patients and Number of Prescriptions per Antibiotic in the Vascular Ward in 2013.....69
Table 16: World Health Organization Defined Daily Dose (DDD) versus Prescribed Daily Dose (PDD) for Antibiotics in the Vascular Ward in 2013.....70
Table 17: The Daily Cost and Total Utilization Cost of Antibiotics per Patient in the Orthopaedic Ward in 2013.....73
Table 18: The Average Daily Cost, Number of Days and Total Utilization Cost per Antibiotic in the Orthopaedic Ward in 2013.....74
Table 19: The Daily Cost and Total Utilization Cost of Antibiotics per Patient in the Vascular Ward in 2013.....75

Table 20: The Average Daily Cost, Number of Days and Total Utilization Cost per Antibiotic in the Vascular Ward in 2013 76
Table 21: The Microscopy, Culture and Sensitivity and Total Costs of the NHLS Laboratory Tests conducted that isolated MRSA per patient in the Orthopaedic Ward in 2013....77
Table 22: The Microscopy, Culture and Sensitivity and Total Costs of the NHLS Laboratory Tests that isolated MRSA per patient in the Vascular Ward in 2013 78
Table 23: **Variables used in the Decision-Tree-Analytic Models for the Orthopaedic Ward** 84
Table 24: Variables used in the Decision-Tree-Analytic Models for the Vascular Ward 85
Table 25: Rankings for the Decision-Tree-Analytic Models run with Actual and then Equal Probabilities in the Orthopaedic and Vascular Ward 91
Table 26: The Expected Value of the Payoffs and the Path Probabilities for the Decision-Tree-Analytic Models in the Orthopaedic Ward....92
Table 27: The Expected Value of the Payoffs and the Path Probabilities for the Decision-Tree-Analytic Models in the Vascular Ward....93
Table 28: The Overall Reported Range of *Staphylococcus aureus* Resistance to Beta-lactam Antibacterial Drugs (MRSA) Obtained from Data Sources in Various Regions (Adapted from: World Health Organization, 2014, Table 7)...108
Table 29: Summary of the Database Medsas-contract-prices-INN-ATC 2013 Reflecting the Antibiotics used in the Orthopaedic Ward 144
Table 30: Summary of the Database Medsas-contract-prices-INN-ATC 2013 Reflecting the Antibiotics used in the Vascular Ward 145
Table 31: NHLS List of Prices of the Different Steps Used for the Laboratory Tests Conducted that Isolated MRSA in the Study Population in the Orthopaedic Ward 146
Table 32: NHLS List of Prices of the Different Steps Used for the Laboratory Tests Conducted that Isolated MRSA in the Study Population in the Vascular Ward 147
Table 33: Price of Cepheid Xpert MRSA Kits from the Quote Requested and Received (QT1005SP)....149
Table 34: Detailed Codes and Categories Identified from the Ethnographic Observations in the Clinical Wards....150
Table 35: Detailed Codes and Categories Identified from the Ethnographic Observations in the NHLS Microbiology Laboratory 151

Table 36: Detailed Codes and Categories Identified from the Ethnographic Observations in the Antibiotic Dispensary 153
Table 37: The Daily Cost and Total Utilization Cost for Each Antibiotic Administered to Each Patient in the Orthopaedic Ward in 2013 154
Table 38: The Daily Cost and Total Utilization Cost for Each Antibiotic Administered to Each Patient in the Vascular Ward in 2013 156
Table 39: Cost of Each NHLS Laboratory Test that Isolated MRSA per Patient in the Orthopaedic Ward in 2013 159
Table 40: Cost of Each NHLS Laboratory Test that Isolated MRSA per Patient in the Vascular Ward in 2013 161
Table 41: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted that Isolated MRSA per Patient in the Orthopaedic Ward in 2013 163
Table 42: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted that Isolated MRSA per Patient in the Vascular Ward in 2013 164
Table 43: Threshold Analysis for the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward 170
Table 44: Threshold Analysis for the Actual Decision-Tree-Analytic Model in the Vascular Ward 170
Table 45: Threshold Analysis for the Equal Decision-Tree-Analytic Model in the Orthopaedic Ward 171
Table 46: Threshold Analysis for the Equal Decision-Tree-Analytic Model in the Vascular Ward 171

LIST OF FIGURES

Figure 1: Study Design Showing Mixed Methods Research: Qualitative Methods used to Inform Quantitative Methods 25

Figure 2: Breakdown of the Number of Samples and Patients that Isolated MRSA at CMJAH in 2013 to Determine the Study Population 27

Figure 3: Decision-Tree-Analytic Model Structure Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward 36

Figure 4: Decision-Tree Analytic Model Structure Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward 39

Figure 5: Various Clinical Aspects Observed in the Orthopaedic and Vascular Wards 52

Figure 6: Steps Involved in the Conventional Culture Method 55

Figure 7: Process Involved in the Planting Step 56

Figure 8: Process Involved in the Microscopy Step 56

Figure 9: Process Involved in the Culture Step 57

Figure 10: Process Involved in the Picking Step 58

Figure 11: Process Involved in the Antibiotic Sensitivity Step 58

Figure 12: Types of Specimens Taken that Isolated MRSA in the Orthopaedic Ward in 2013 72

Figure 13: Types of Specimens Taken that Isolated MRSA in the Vascular Ward in 2013 72

Figure 14: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted per Patient in the Orthopaedic Ward in 2013 81

Figure 15: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted per Patient in the Vascular Ward in 2013 82

Figure 16: Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward 87

Figure 17: Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward 88

Figure 18: Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward 89

Figure 19: Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward 90

Figure 20: One-Way Sensitivity Analysis Graph for the Variable cDailyEmpiricAntibiotic in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward 95

Figure 21: One-Way Sensitivity Analysis Graph for the Variable cDailyMrsaSpecificAntibiotic in the Actual Decision-Tree-Analytic model in the Orthopaedic Ward 95
Figure 22: One-Way Sensitivity Analysis Graph for the Variable cSpecimenCS in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward 96
Figure 23: One-Way Sensitivity Analysis Graph for the Variable cSpecimenM in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward 96
Figure 24: One-Way Sensitivity Analysis Graph for the Variable cXpertMRSA in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward 97
Figure 25: One-Way Sensitivity Analysis Graph for the Variable pSpecimenSentMCS in the Equal Decision-Tree-Analytic Model in the Orthopaedic Ward 97
Figure 26: One-Way Sensitivity Analysis Graph for the Variable cDailyOtherAntibiotic in the Actual Decision-Tree-Analytic Model in the Vascular Ward 99
Figure 27: One-Way Sensitivity Analysis Graph for the Variable cDailyMrsaSpecificAntibiotic in the Actual Decision-Tree-Analytic Model in the Vascular Ward 99
Figure 28: One-Way Sensitivity Analysis Graph for the Variable cXpertMRSA in the Actual Decision-Tree-Analytic Model in the Vascular Ward 100
Figure 29: One-Way Sensitivity Analysis Graph for the Variable cDailyEmpiricAntibiotic in the Actual Decision-Tree-Analytic Model in the Vascular Ward 100
Figure 30: One-Way Sensitivity Analysis Graph for the Variable cDailyEmpiricAntibiotic in the Equal Decision-Tree-Analytic Model in the Vascular Ward 101
Figure 31: One-Way Sensitivity Analysis Graph for the Variable pMrsaIsolated in the Equal Decision-Tree-Analytic Model in the Vascular Ward 101
Figure 32: One-Way Sensitivity Analysis Graph for the Variable pSpecimenSentMCS in the Equal Decision-Tree-Analytic Model in the Vascular Ward 102
Figure 33: Tornado Diagram for the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward 103
Figure 34: Tornado Diagram for the Actual Decision-Tree-Analytic Model in the Vascular Ward 104
Figure 35: Tornado Diagram for the Equal Decision-Tree-Analytic Model in the Orthopaedic Ward 105
Figure 36: Tornado Diagram for the Equal Decision-Tree-Analytic Model in the Vascular Ward 105

Figure 37: Rollback of Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward 166
Figure 38: Rollback of Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward 167
Figure 39: Rollback of Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward.....168
Figure 40: Rollback of Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward.....169

ABBREVIATIONS

ATC: Anatomical Therapeutic Chemical

CS: Culture and Sensitivity

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

DDD: Defined Daily Dose

DRI: Debridement, Reaming and Irrigation

FOX: Cefoxitine

HAI: Hospital-Acquired Infection

HCP: Healthcare Professional

ICU: Intensive Care Unit

IV: Intravenous

MCS: Microscopy, Culture and Sensitivity

MRSA: Methicillin-Resistant *Staphylococcus aureus*

NHLS: National Health Laboratory Service

PCR: Polymerase Chain Reaction

PDD: Prescribed Daily Dose

PPE: Personal Protective Equipment

PVD: Peripheral Vascular Disease

R: Rands

SAASP: South African Antibiotic Stewardship Programme

STG: Standard Treatment Guidelines

UPFS: Uniform Patient Fee Schedule

WHO: World Health Organization

1. INTRODUCTION

1.1 Background to Research

Hospital-Acquired Infections (HAIs) are a prevalent problem in hospitals worldwide. In South Africa, it is predicted that one in seven patients are at a high risk of HAIs (Brink *et al.*, 2006). Infection due to MRSA is amongst the most common HAIs and ranges from an asymptomatic infection to one that can be fatal (Cunningham *et al.*, 2007).

HAIs increase patient mortality and morbidity as well as increase the cost of patient care, therefore, infection control policies are established to prevent and reduce these infections. However, within South African hospitals, these policies are not always strictly adhered to (Brink *et al.*, 2006). Infection control policies can consist of routine contact precaution, isolation, decolonization, screening and surveillance (Girou *et al.*, 1998; Rebmann *et al.*, 2011). Screening and testing for HAIs can be performed using various methods.

The Conventional Culture Method is commonly used when an MRSA infection is suspected. However, in using this method, it can take between one and five days to confirm an MRSA infection. The range in waiting time is due to the required methodology of the Conventional Culture Method, in which microscopy is first performed to identify Gram-positive cocci, followed by incubation for 24 and 48 hours and thereafter, further incubation and antibiotic sensitivity tests (Huletsky *et al.*, 2004; Brown *et al.*, 2010). It is general practice to administer empiric antibiotics whilst Healthcare Professionals (HCP) are waiting for the patient's test results. These are broad-spectrum antibiotics with the aim of targeting the most probable organisms causing the infection. Empiric antibiotics are often expensive and may lead to unnecessary antibiotic usage, which could then lead to further antibiotic resistance. Only once the test results are available can the HCP change the antibiotics to a narrow spectrum and targeted treatment, thus the prolonged waiting period for the test results causes a delay in optimum targeted patient therapy (Cunningham *et al.*, 2007; Kluytmans, 2007).

Although the Conventional Culture Method has been routinely used to identify suspected infections, alternative methods are being investigated due to having to wait for up to five days before the patient's confirmed tests results are available. One of the novel methods under consideration to identify MRSA is to use real-time PCR testing. These tests are becoming more favoured as the laboratory testing process is less labour-intensive and MRSA test results are available within two hours (Kluytmans, 2007). The tests therefore eliminate the need for empiric antibiotics and targeted therapy can be initiated sooner to eradicate the patient's infection, thereby reducing further transmission of MRSA and ultimately decreasing morbidity and mortality due to MRSA (Wolk *et al.*, 2009).

Despite the numerous benefits of the novel PCR testing for MRSA, cost is a disadvantage of the PCR tests, as this method is more expensive than the Conventional Culture Method. International studies comparing the costs of using the Conventional Culture Method to the PCR testing methods have demonstrated that the rapid PCR tests may be more cost-saving due to the benefits of the rapid release of PCR test results (French, 2009; Li *et al.*, 2012). Cost studies comparing the cost and treatment outcomes from the use of Conventional Culture Method to PCR tests for MRSA resistance have not yet been conducted in South Africa. The outcomes of such studies could greatly assist in decision-making when updating infection control policies to implement new screening or diagnostic methods that would be beneficial to both patients and healthcare institutions.

There are published guidelines for the treatment of patients with MRSA in South African public sector hospitals (Department of Health, 2012). However, no detailed evidence could be found regarding the actual clinical management pathways, and associated costs, that follow in daily practice for these patients. Thus, to inform the decision-tree-analytic models, this study includes conducting observations to document the current clinical management of MRSA at a public hospital in South Africa.

Decision-analytic modelling is a useful tool for assessing alternatives and therefore economic evaluations using decision-analytic modelling are becoming increasingly popular to inform decision-making in healthcare. Studies have developed decision-analytic models to compare the costs and management pathways that follow when using the Conventional Culture Method versus PCR testing for MRSA (Li *et al.*, 2012; Tübbicke *et al.*, 2012a).

However, a search of the literature shows that, such decision-tree-analytic models have not yet been built for the South African healthcare context. It is important that these models are developed in relation to healthcare in South Africa as the country's socio-economic status and access to healthcare may contribute different influences as compared with other countries (Ataguba *et al.*, 2011).

Therefore, there is a need for research to be conducted in the South African healthcare context to build decision-tree-analytic models comparing the costs and management pathways that follow depending on whether the Conventional Culture Method or PCR tests are used for MRSA to inform future decision-making. This research aims to create such models for use in varying healthcare situations in order to compare alternatives to aid in decision-making in any public hospital in South Africa.

1.2 Aim

The aim of this study was to investigate the management pathways and associated costs of using the current Conventional Culture Method for MRSA testing, to construct decision-tree-analytic models and compare them to the new PCR testing, in order to inform future decision-making.

1.3 Objectives

1. To conduct observations in selected hospital wards in order to document the clinical practices of HCPs regarding the current management of patients with suspected MRSA infection; to identify the current methods used to detect MRSA at the microbiology laboratory; and to document the process of dispensing antibiotics to inpatients at the antibiotics designated area of the main CMJAH dispensary.

2. To carry out a retrospective utilization review of the different antibiotic regimes administered and laboratory tests conducted that isolated MRSA in the study population.

3. To perform a cost analysis, using the utilization and costing data obtained, to determine the costs associated with the antibiotics administered and laboratory tests conducted that isolated MRSA in the study population.

4. To develop decision-tree-analytic models to compare the current costs and management pathways associated with the Conventional Culture Method versus a theoretical scenario arising if the PCR tests for MRSA were to be implemented at CMJAH.

2. LITERATURE REVIEW

2.1 Hospital-Acquired Infections

2.1.1 Overview of Hospital-Acquired Infections

Globally developing and developed countries are affected by HAIs. It is predicted that within South African hospitals, one in seven patients are at a high risk of HAIs (Brink *et al.*, 2006). HAIs are not only a common occurrence but also a critical problem as they are a major cause of death, increased morbidity and additional costs within hospitals (Calfee, 2012; Kelly *et al.*, 2012).

HAIs, also known as nosocomial infections, are defined as, “An infection acquired in hospital by a patient who was admitted for a reason other than that infection”. If the infection was not incubating or present when the patient was admitted to hospital but develops 48 hours thereafter, it is classified as an HAI. Infections that occur within four weeks after hospital discharge are also termed HAIs. HAIs may also include visitors or hospital personnel that acquire infections (World Health Organization, 2002).

2.1.2 Types of Hospital-Acquired Infections

HAIs can be identified using definitions formulated from biological and clinical measures for specific infection sites. There are around 50 possible sites of infection, the most common of which are the urinary tract, respiratory tract, skin and soft tissue as well as surgical sites. There are also different routes of transmission for micro-organisms that cause infection in hospitalised patients. Bacteria can be transmitted by direct contact between patients and HCPs or by indirect contact from objects contaminated with micro-organisms, as well as via droplet or airborne spread. HAIs may also be caused by a disruption in the patient’s own flora or by bacterial resistance that develops due to commonly used antibiotics (World Health Organization, 2002; Brink *et al.*, 2006).

HAIs may be caused by various pathogens. Depending on the country, hospital environment, patient population and other factors, the type and frequency of pathogens may differ. However, most HAIs are caused by bacteria, such as *Staphylococcus aureus*, *Enterobacteriaceae* and *Pseudomonas* species. Data reported to the National Healthcare Safety Network between 2009 and 2010 regarding antimicrobial resistant pathogens accountable for HAIs revealed that of all the pathogens reported, 16% of the pathogens were due to *Staphylococcus aureus*, 14% due to *Enterococcus* species, 12% due to *Escherichia coli*, 11% due to coagulase-negative staphylococci, 9% due to *Candida* species, 8% due to *Pseudomonas aeruginosa* and 5% due to *Enterobacter* species. These HAIs include ventilator-associated pneumonia, catheter-associated urinary tract infections, surgical site

infections and central line–associated bloodstream infections. Amongst the reported pathogens responsible for all the HAIs, approximately 20% of the pathogens were multidrug-resistant phenotypes and as such, MRSA accounted for 8.5%, vancomycin-resistant *Enterococcus* accounted for 3%, *Escherichia coli, Enterobacter* species and carbapenem-resistant *Pseudomonas aeruginosa* each accounted for 2%. This was the second antimicrobial susceptibility report of data from the National Healthcare Safety Network and when comparing the resistance data of the first and second reports, the findings stated above were similar (Sievert *et al.*, 2013).

2.1.3 Factors that Promote Infection in Hospitalised Patients

Patients staying in hospitals are vulnerable to acquiring infections. Factors that predispose these patients to infection include having a weakened immune system; undergoing medical procedures and the insertion of invasive medical devices; having open wounds; receiving glucocorticosteroid and antibiotic medication; and non-adherence to infection control policies (Yamakawa *et al.*, 2011). Studies have established that within hospitals, the Intensive Care Unit (ICU), acute surgical and orthopaedic wards have the highest prevalence of HAIs (World Health Organization, 2002).

2.1.4 Impact of Hospital-Acquired Infections

HAIs hinder the patient, the hospital and the economy as these infections unnecessarily increase the morbidity and mortality rate and add to the cost of patient care within hospitals. Patients that are affected with HAIs are at a higher risk of medical complications and co-morbidities that may last throughout their life (World Health Organization, 2002).

A common consequence of HAIs is increased length of patient stay in hospital. Studies conducted show various results for prolonged length of stay due to different methods used to calculate these values as well as the type of HAIs and wards that were included in the study. One study found that increased length of stay and costs due to HAIs in patients with lower respiratory tract infections was 2.58 extra days in hospital, whereas a patient with a urinary tract infection would not have any additional days in hospital (Graves *et al.*, 2007). This contrasts with a study conducted by Schulgen and co-authors, which used different approaches that reflected an increased length of stay due to HAIs, as the estimated number of extra days for patients with post-operative wound infection was 21, 11 and 10 to 12 days, and for patients with nosocomial pneumonia length of stay was 14, 8 and 3 to 4 extra days. The variation in the numbers reported is due to the different methods used to calculate the extra number of days spent in hospital due to HAIs (Schulgen *et al.*, 2000).

Additional number of days spent in hospital due to HAIs greatly increases the cost of patient care. Other costs that are associated with HAIs are increased labour costs, administration of additional medication, further laboratory tests and extra infection control precautionary measures required. In a study that estimated the increase in healthcare costs due hospital-acquired bloodstream infections, the additional costs attributable were: increased length of stay (58% of total costs); antibiotics and other pharmaceutical products (each 10% of total cost); billed medical procedures (15% of total cost); and laboratory tests (2.4% of total cost) (Vrijens *et al.*, 2010). Another study reported that the costs for patients with HAIs are up to two and a half times higher than the costs for patients without HAIs (Glance *et al.*, 2011). Thus it can be seen that these preventable HAIs unnecessarily use up scarce resources that are allocated to hospitals.

This study focuses on MRSA, which is a bacterial pathogen that is resistant to commonly used antibiotics.

2.2 Methicillin-Resistant *Staphylococcus aureus*

2.2.1 Overview of MRSA

Staphylococcus aureus is a Gram-positive facultative anaerobic bacterium. In humans it can be found in normal bacterial flora or it can present as pathogenic which causes infections. In the late 1950s, methicillin was developed and was used to treat *Staphylococcus aureus*. However, shortly thereafter in 1960, methicillin resistance emerged (Kelly *et al.*, 2012). MRSA is a strain of *Staphylococcus aureus* which is resistant to commonly used beta-lactam antibiotics including methicillin, oxacillin, amoxicillin and penicillin (Gorwitz *et al.*, 2008). MRSA is a leading cause of many HAIs but is also present in the community and amongst people with no known risk factors. However, this study focuses only on Hospital-Acquired MRSA.

A literature review by Tübbicke and co-authors (2012b) provides an overview of the key factors that need to be taken into account when considering the burden and cost of MRSA as well as when deciding on which MRSA screening method to implement. These key factors include the prevalence and transmission rate of MRSA; the costs of each case of MRSA; and the performance characteristics, turn-around-time and cost of the various methods of screening for MRSA. Therefore, MRSA infections are a complex challenge within hospitals (Tübbicke *et al.*, 2012b).

2.2.2 Prevalence of MRSA

The prevalence of Methicillin-Resistance amongst *Staphylococcus aureus* clinical isolates in Africa was evaluated in a literature review published in 2013. The data extracted in this

review indicates that from 2006 to 2011, the prevalence of MRSA among *Staphylococcus aureus* isolates decreased from 36% to 24% in South Africa. This is in contrast to data extracted for many other countries in Africa where the prevalence of MRSA seems to have increased since 2000 (Falagas *et al.*, 2013). It is important to note that in these studies the rate of MRSA is expressed as the percentage of MRSA amongst *Staphylococcus* aureus isolates only and not as a percentage of all isolates obtained in that period.

A retrospective study looking at patients with *Staphylococcus aureus* bacteraemia at Chris Hani Baragwanath Academic Hospital and at CMJAH between November 1999 and October 2002 reported that the prevalence of MRSA was 23.4% (105 of 449 patients with *Staphylococcus aureus* bacteraemia) and that within a period of fourteen days there was a mortality rate of 33.3% in these patients suffering with MRSA bacteraemia (Perovic *et al*., 2006).

In comparison, a 26.9% MRSA rate was measured in a retrospective study carried out at 14 provincial hospitals in KwaZulu-Natal from March to August 2001 and from October 2002 to August 2003. This study analysed 227 *Staphylococcus aureus* isolates and 61 of them were found to be resistant to oxacillin, methicillin and cefoxitin. It was also reported that resistance to six antibiotics classes was present amongst more than 40% of the MRSA isolates and resistance to a minimum of four antibiotic classes was identified in more than 80% of the MRSA isolates (Shittu *et al.*, 2006).

Furthermore, a 36% MRSA national incidence rate was revealed in a study investigating the antimicrobial susceptibility profiles of *Staphylococcus aureus* and other bacteraemic pathogens in South African private hospitals. This study used blood cultures isolated from patients in private hospitals in Johannesburg, Pretoria, Durban, Cape Town and Bloemfontein. Twelve laboratories were used to perform the antimicrobial susceptibility tests during the first six months of 2006. From the total of 25 524 blood culture isolates tested, 629 were *Staphylococcus aureus* isolates and the average prevalence of oxacillin resistance was 36%. This study also demonstrates that the demographic distribution of MRSA fluctuates from 29% to 46% within different private hospitals in South Africa (Brink *et al.*, 2007).

Currently, the latest available published data shows a 24% MRSA rate amongst *Staphylococcus aureus* isolates. This was found in a study conducted to determine the genetic basis of rifampicin resistance amongst isolates of MRSA in Cape Town hospitals. From July 2007 to June 2011, 13 746 *Staphylococcus aureus* isolates were obtained from the Groote Schuur Hospital NHLS Laboratory. Antimicrobial susceptibility tests were then

conducted and 3 298 (24%) of these isolates were found to be MRSA (Jansen van Rensburg *et al.*, 2012).

The different studies also used varying methods of identifying the isolates and in some cases the isolates were collected from private institutions as well. The methodology used in the studies needs to be taken into account in order to understand the implications of the percentage of MRSA expressed. However, despite the differences in the above studies, an overall decrease in the prevalence of MRSA in South Africa can be seen (33.3% in 1999; 24% in 2011). Nonetheless, it is still important to research new methods of MRSA testing to further decrease this prevalence as well as to decrease the cost, mortality and morbidity currently associated with MRSA.

2.2.3 Clinical Manifestation of MRSA

It is important to be familiar with the manner in which MRSA presents clinically in order to recognise a suspected MRSA infection based on the signs and symptoms of a patient. Once MRSA is suspected, a series of steps need to be taken.

Unlike some HAIs, infections due to MRSA do not present clinically with clear defining characteristics. HA-MRSA can cause bacteraemia, urinary tract infections, gastroenteritis, endocarditis, pneumonia, osteomyelitis and skin infections such as abscess, necrotising fasciitis, cellulitis and surgical site infections. The type of infection caused by HA-MRSA is influenced by the site of inoculation, toxins produced and virulence factors. Although MRSA infections are not defined by specific clinical features, there are certain risk factors that can assist when suspecting an MRSA infection. Risk factors include length of stay in hospital, being immunocompromised, previous infections, surgery and insertion of medical devices (Naimi *et al.*, 2003; Kelly *et al.*, 2012).

To further guide the diagnosis of MRSA, the patient's history, antibiotic prescriptions and surgical procedures should be considered as well as local epidemiological trends should be taken into account. As infections due to MRSA cannot easily be diagnosed by clinical manifestations, laboratory diagnostic tests have to be done to confirm MRSA infections. Once an infection due to MRSA is suspected, samples from the patient need to be sent to the microbiology laboratory for investigation, empiric antibiotics are initiated and increased contact precaution measures should be implemented to prevent contamination and transmission of MRSA to other patients in the ward as well as to HCPs and visitors

2.2.4 Transmission and Colonization of MRSA

HA-MRSA can be transmitted in the same manner in which other HAIs are transmitted, such as through droplet spread, contaminated objects and infected patients. Additionally, *Staphylococcus aureus* is a colonizer of various sites in humans, the nose being the most common, as 20% to 30% of the general population are nasal carriers of *Staphylococcus aureus*. Medical procedures often disturb patients' natural barriers and thus may lead to infection. Therefore, there is controversy over whether eradication of *Staphylococcus aureus* in carriers decreases the risk of pathogenic infection due to *Staphylococcus aureus* and whether there is an increased risk of infection due to *Staphylococcus aureus* in patients that are nasal carriers of *Staphylococcus aureus* (Wertheim *et al.*, 2005).

As most carriers of *Staphylococcus aureus* present asymptomatically and have an increased risk of acquiring an infection while in hospital, many infection control programmes include nasal surveillance of *Staphylococcus aureus* upon hospital admission and decolonization with a topical antibiotic (Nelson *et al.*, 2010).

2.3 Preventing and Managing MRSA

2.3.1 Infection Control

Due to the nature and consequences of infection with MRSA, healthcare institutions try to prevent the emergence and subsequent spread of this pathogen along with many other nosocomial pathogens by devising and implementing strategies commonly referred to as Infection Control Policies. Infection control policies consist of various mandatory protocols for HCPs to act in a certain manner when performing their routine tasks. The contents and inclusion of protocols differs between various areas of the hospital as well as between different healthcare institutions. Common infection control practices are: routine contact precaution or barrier nursing such as hand hygiene practices; decontamination of equipment and surroundings; pre-emptive isolation of suspected MRSA-infected patients and isolation of MRSA-positive patients; decolonization of patients; and surveillance including screening of patients for MRSA (Girou *et al.*, 1998; Rebmann *et al.*, 2011).

Within healthcare institutions, MRSA infection control policies can be divided into two broad strategies: surveillance and contact precaution measures. Each strategy consists of many programmes which may be used and the types of programmes chosen vary widely between institutions. Various studies have been conducted to evaluate the effectiveness of these programmes within hospitals in an attempt to formulate optimal guidelines to implement. The alternative programmes in each strategy are explained below.

Surveillance can take place in the form of universal surveillance or targeted surveillance. The classification and definitions of the types of surveillance vary. Universal surveillance is when all patients admitted to a hospital are screened for all types of pathogens, whereas targeted surveillance is restricted to screening only those patients that are seen as high risk patients, or to certain areas of the hospital (Tübbicke *et al.*, 2012a). Targeted surveillance, also known as active surveillance, can include screening all patients when they are admitted to hospital, but it is screening for a specific pathogen such as MRSA only. Specimens collected based on patient's presenting with signs and symptoms of infection are part of passive or clinical surveillance (Rebmann *et al.*, 2011; Edmond *et al.*, 2013). Certain hospitals focus on selective screening of MRSA nasal carriers on admission as they are at risk of developing into subsequent infections (Girou *et al.*, 1998). In large hospitals and when resources are limited it is not feasible to screen all patients that are admitted, therefore it is important to be able to identify the risk factors in patients and high risk areas within the hospital.

Contact precaution measures need to be initiated for patients that have been identified as MRSA-positive or are suspected to be infected with MRSA, in order to prevent the transmission of the pathogen. The World Health Organization (WHO) has formulated a list of precautions that should be implemented to prevent the spread of MRSA and certain countries have developed their own infection control organizations which have produced specific guidelines for their hospitals to follow. However, most of the guidelines include the following steps: early detection of infection; isolating infected or colonised patients either in an isolation ward or pre-emptive isolation of patients with suspected MRSA infection; decreased ward transfers and vigilance of patients from other hospitals; skin decolonization using chlorhexidine or mupirocin for nasal carriers; hand hygiene campaigns and using an alcohol-based disinfectant frequently; barrier precaution of wearing gloves, masks and aprons when interacting with MRSA infected patients or equipment; decontamination of medical devices and the environment as well as proper disposal of medical waste. (World Health Organization, 2002; Huang *et al.*, 2006; Rebmann *et al.*, 2011; Moody *et al.*, 2013).

It is evident that there are numerous methods available to prevent the transmission of MRSA. Unfortunately, these policies are not always strictly adhered to and are practised to a variable extent amongst different hospitals and HCPs. Therefore, it is important to evaluate these policies and understand why certain of them are not carried out correctly in order to enhance the current policies and develop novel methods within these policies (Moody *et al.*, 2013). In order to develop successful MRSA infection control policy, all members in the healthcare institution need to be incorporated and support from hospital management is essential (Rebmann *et al.*, 2011). When deciding which programmes would be most suitable to

implement in a healthcare institution, various factors need to be taken into account: cost and access to resources are commonly an important consideration.

2.3.2 Infection Control in South Africa

Around the world, countries are developing, improving and implementing infection control policies to reduce the number of infections within healthcare institutions due to the negative impact of these infections. The Department of Health in South Africa developed *The National Infection Prevention and Control Policy and Strategy 2007,* in order to support the WHO Global Patient Safety drive. The purpose stated in this policy is, "to set minimum national standards for the effective prevention and management of health care associated infections". This document outlines the roles and responsibilities of the various HCPs in healthcare institutions, provides a summary of the areas identified for improvement and includes other factors that need to be considered when developing a successful infection prevention and control policy (Department of Health, 2007).

Although infection control policies are available globally, the South African public healthcare system faces numerous challenges such as: infection control policies are not well established and are practised inconsistently within different institutions; data is often under-reported or not reported from all hospitals and laboratories; and standardised surveillance systems are not implemented in the majority of these institutions. Currently, inadequate infection control practices are also due to medical equipment not being disinfected correctly, transfer of colonised or infected patients between hospitals, overcrowding in healthcare facilities and administering parenteral fluids that are contaminated. Additional problems are staff shortages and overworked staff for the large amount of patients, inadequate training and supervision of staff and limited numbers of correctly qualified infection control practitioners (Dusé, 2005). It is important that effective infection control policies, surveillance systems and infection prevention and control training programmes are enforced in all South African healthcare institutions. Therefore, in 2005, *The Guideline for the Management of Nosocomial Infections in South Africa* was published, outlining the management of common nosocomial infections by providing their definition, microbiology, diagnosis, management, duration of treatment and prevention, as it aims to "provide recommendations for the initial choice of antimicrobial agents and the appropriate management of these infections" (Brink *et al.*, 2006).

2.3.3 Antibiotic Treatment Pathways

Within South African public hospitals and clinics, The Standard Treatment Guidelines (STG) and Essential Medicines List are commonly used as a reference amongst HCPs when prescribing and administering medication. According to this guideline intravenous (IV)

vancomycin at a dose of 20 mg/kg every 12 hours is administered to patients with MRSA infection. It is also recommended that after the third dose of vancomycin the patient's trough levels should be monitored and the dose must then be adjusted accordingly to ensure that the trough level stays between 15–20 micromol/L (Department of Health, 2012).

Although vancomycin can be seen as the current "gold standard" for the treatment of MRSA infections, alternative antimicrobials such as linezolid, trimethoprim-sulphamethoxazole, clindamycin, daptomycin, quinupristin/dalfopristin and tigecycline as well as novel agents may be considered for the treatment of MRSA infections due to the emergence and rise of vancomycin-resistant *Staphylococcus aureus* (Micek, 2007; Wasserman *et al.*, 2011). It is therefore imperative that antibiotic programmes are executed in hospitals to decrease and prevent further antibiotic resistance.

In an attempt to standardise, monitor and compare the utilization of medication, including antibiotics, the WHO has formulated the Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) system. The DDD is the "assumed average maintenance dose per day for a drug used for its main indication in adults" and is used as an international measurement unit for drug utilization research (World Health Organization Collaborating Centre for Drug Statistics Methodology, 2012). Due to the contribution of incorrect antibiotic use to increasing antibiotic resistance, studies have used the DDD to measure and compare antibiotic consumption in hospitals (Muller *et al.*, 2006; Gagliotti *et al.*, 2014).

Antibiotics are commonly prescribed and administered inappropriately. Therefore, to further guide HCPs when prescribing and administering antibiotics, Antibiotic Stewardship programmes are devised and implemented in healthcare institutions to promote and ensure the proper use of antibiotics to try to decrease and prevent further resistance. South African Antibiotic Stewardship programmes include the MCC Conference on Antimicrobial Resistance, Global Antibiotic Resistance Partnership South Africa, South African Antibiotic Stewardship Programme (SAASP) and the Best Care…Always! Campaign (Dusé, 2005; Dusé, 2011). Recently, the South African Antimicrobial Resistance National Strategy Framework 2014-2024 was developed by the National Department of Health with aid of the SAASP and WHO. This framework consists of three pillars which are: Antimicrobial Stewardship; Antimicrobial Surveillance; Infection Prevention and Control. This framework also encourages research in diagnostic and therapeutic agents within South Africa (Mendelson *et al.*, 2015).

When managing a patient with an MRSA infection or suspected infection, various factors should be considered before simply prescribing the first line standard treatment available.

These factors include the source of the patient's infection, for example, if it is a deep wound infection then antibiotics and a drainage system may be required. The results of the microbiology laboratory diagnostic tests are another factor that should be used to guide the choice of antibiotic treatment for the individual patient (Wasserman *et al.*, 2011). However, while HCPs are waiting for these results from a patient suspected to be infected with MRSA, a common strategy is to administer empiric treatment to the patient. Empiric treatment includes administering a broad-spectrum antibiotic which would act against the most probable causes of infection. While this may seem effective, empiric antibiotics are usually expensive and may result in unnecessary use of antibiotics which could lead to further organism resistance (Cunningham *et al.*, 2007; Kluytmans, 2007). Therefore, novel rapid ways of testing for MRSA are being investigated to decrease the problems encountered while waiting for current the microbiology diagnostic tests used.

2.4 Laboratory Tests for MRSA

2.4.1 Screening versus Diagnostic

Methods for detecting MRSA and other pathogens can be used for screening as part of a surveillance programme or as diagnostic tests to guide a patient's clinical diagnosis. Within a surveillance programme there are various forms of screening that can be performed, such as active screening (Muto *et al.*, 2003), universal screening, routine screening (Huang *et al.*, 2006), selective screening (Girou *et al.*, 1998) or a combination of these and other screening methods. Globally, many healthcare institutions screen their patients on admission to detect carriers for MRSA and/or other pathogens, as these carriers are at potential risk of developing and spreading infections. Therefore, this strategy is to rapidly identify carriers so that they can be decolonised and appropriate contact precaution can be implemented (Davis *et al.*, 2004). Currently, there is much controversy regarding the effectiveness of such screening programmes (McGinigle *et al.*, 2008; Edmond *et al.*, 2013; Glick *et al.*, 2014). However, not all healthcare institutions screen their patients on admission due to various reasons such as cost, limited resources and insufficient staff. These healthcare institutions would then only conduct diagnostic tests when a specific patient presents with clinical signs and symptoms of a suspected infection (Harbarth *et al.*, 2011).

There are various methods available to detect for MRSA and the same methods can be used for either screening or diagnostic tests. This study focuses on the Conventional Culture Method and the new PCR testing for MRSA infections.

2.4.2 Conventional Culture Method

Although the Conventional Culture Method is most commonly used to detect MRSA in patients, it takes a period of between one to five days before the results reflecting a patient's

MRSA status are available. Even though this method is quite sensitive for detecting MRSA, the prolonged waiting time is problematic in many aspects. While waiting for the laboratory results from the Conventional Culture tests, empiric antibiotics are often prescribed and administered to patients with a suspected infection. The use of these empiric antibiotics needs to be investigated and strictly controlled as their misuse may lead to additional resistance, increased costs and unnecessary use of limited resources. The waiting period also delays the initiation of optimum targeted therapy for patients. Another problem that occurs while waiting for the culture results is that in settings where all suspected patients are isolated there is lengthy unnecessary isolation of patients, as only about 5% of these patients would actually be carriers of MRSA. In settings where patients are isolated only after culture results are available, there is an increased risk of transmission of MRSA as the MRSA infected patient would be amongst other patients during the waiting period (Cunningham *et al.*, 2007; Kluytmans, 2007).

The detection of organisms using the culture method in microbiology laboratories is a complex process that requires numerous equipment and sequential steps to be followed. Various studies have been conducted using alternative equipment and variations of the steps in the methodology in an attempt to increase the sensitivity and specificity of the tests as well as to decrease the turn-around-time for the culture results. Some studies have developed and used numerous types of different agar or media and are then compared with the results to determine which agar or media produced the best results (Malhotra-Kumar *et al.*, 2010). It has also been shown that variations in the incubation time affect the results of the culture tests (van Hal *et al.*, 2007). Alternative studies have compared different types of nasal swabs and how they respond to the various agars and incubation techniques to deduce the best combination (Safdar *et al.*, 2003). The standard culture method used in certain laboratories is to plate directly on the agar media, while in other laboratories broth enrichment occurs before plating (Nonhoff *et al.*, 2009; Harbarth *et al.*, 2011; Marlowe *et al.*, 2011).

Thus the standard laboratory methods used for the detection of organisms by culture differ between laboratories and institutions. In South Africa, the NHLS is the public diagnostic pathology laboratory that provides services for more than 80% of the population (Bekker *et al.*, 2014). The NHLS is a member of the Clinical Laboratory Standards Institute which has standard guidelines that should be followed when conducting laboratory tests.

2.4.3 PCR Testing Method

Due to the consequences of waiting for up to five days for the results of the Conventional Culture method, new rapid molecular nucleic acid methods for MRSA screening are being investigated. Real-time PCR testing for MRSA has emerged and is becoming popular as it

produces the patient's MRSA results within two hours (Kluytmans, 2007). The rapid release of results from PCR testing leads to numerous benefits. For example, as the patient's MRSA status will be available in less than two hours, the need for empiric treatment is eliminated and HCPs can immediately administer optimal targeted treatment that aids in the recovery of the patient and decreases the MRSA transmission, thereby decreasing the morbidity and mortality due to MRSA (Wolk *et al.*, 2009). Rapid PCR testing may also reduce unnecessary and costly pre-emptive isolation and allows for prompt isolation and effective decolonization for known MRSA infected patients (Cunningham *et al.*, 2007).

In addition to the mentioned benefits associated with the PCR tests ability to rapidly release the patients' results, the PCR tests are simpler to use and require less hands-on time as compared to the Conventional Culture Method. Certain PCR systems can also be installed directly in the hospital wards. This allows for the PCR tests to be conducted and the results made available directly in the ward, thus decreasing the time delay normally caused by transportation of specimens to the microbiology laboratory and communication between the laboratory and the ward, therefore enabling faster access to MRSA results (Brenwald *et al.*, 2010).

When comparing the cost of the Conventional Culture Method and the new rapid PCR tests, the PCR tests are more expensive. However, international studies have shown that despite the higher cost, the rapid PCR tests may be cost-saving as the test results are available within two hours, which leads to a reduction in empiric antibiotic treatment cost, a decrease in isolation cost, a decline in further MRSA transmission and severity of infections, as well as an increase in targeted optimal healthcare (French, 2009; Li *et al.*, 2012). The results obtained from these studies can positively influence hospital management decisions to implement the method that would be most beneficial to both the patients and the institution.

Studies comparing the cost and treatment outcomes from the use of Conventional Culture Method versus PCR tests for MRSA have not yet been conducted in South Africa. The outcomes of such a study would assist hospitals in South Africa to make decisions on managing MRSA infections, particularly in environments where reducing costs are important due to limited finances.

There are various types of PCR tests for identifying MRSA that are being created and compared. The Xpert MRSA system from Cepheid, the LightCycler MRSA from Roche. and the BD GeneOhm from BD Diagnostics are examples of PCR tests that are approved by the FDA (Marlowe *et al.*, 2011). This study focuses on Cepheid's PCR tests for MRSA. Cepheid is a manufacturing company that has developed and markets novel PCR tests to screen for

Staphylococcus aureus and MRSA in approximately an hour from nasal swabs, blood culture or skin and soft tissue infections using the Cepheid Xpert MRSA, Xpert SA Nasal Complete, Xpert MRSA/SA BC or the Xpert MRSA/SA SSTI assay performed in the GeneXpert System.

2.5 Ethnography in Healthcare

Before a new method is implemented in a hospital, such as the Xpert MRSA testing method for MRSA, it is important to understand and evaluate the current methods and practices that are performed in the hospital setting. One of the manners in which to gain an overview of a healthcare system is to conduct research using both quantitative and qualitative approaches. Ethnography is a qualitative research method which can be defined as, "the study of social interactions, behaviours, and perceptions that occur within groups, teams, organisations, and communities" (Reeves *et al.*, 2008). This definition lends itself well to a hospital setting as HCPs interact with patients and other HCPS, have their own perceptions and practices as well as work with other HCPs as team within the hospital to provide healthcare services to patients.

Therefore, healthcare studies have been conducted which used ethnography to obtain information (Dixon-Woods *et al.*, 2009). A recent study used video-reflex ethnography in two wards within a hospital to make HCPs aware of their current infection control practices in order to identify risk areas and suggest methods of improvement to decrease HAIs (Iedema *et al.*, 2015). Another study used meta-ethnography to analyse HCPs perspectives and practices of antibiotic prescribing in acute respiratory tract infections to determine the reasons that influence interventions to be successful or not (Tonkin-Crine *et al.*, 2011).

A key feature of ethnography is that it includes conducting observations in the natural setting that it being studied to achieve an understanding of the current setting and interactions that are generally not easily identified (Reeves *et al.*, 2008). Ethnography is also used to gain an understanding of the healthcare system, HCPs and patients to assist decision-makers (Goodson *et al.*, 2011).

2.6 South African Healthcare System

2.6.1 Private Sector versus the Public Sector

Healthcare in South Africa is classified as a dual healthcare system as it consists of the private healthcare sector and the public healthcare sector. The private healthcare sector includes private hospitals and general practitioners. Whereas the public healthcare sector includes primary healthcare clinics and Community Health Centres in addition to different levels of hospitals: District (level 1), Regional (level 2) and Central or Tertiary (level 3)

(Coovadia *et al.*, 2009). This study focuses on CMJAH which is an Academic Tertiary Level Hospital in the public healthcare sector in South Africa.

The South African healthcare system is faced with inequalities in the distribution of resources and finances. For example, around 40% of the total health expenditure is used for the public healthcare system which caters for the majority of the population, as more than 60% of the population rely solely on the public healthcare system (Chopra *et al.*, 2009; Coovadia *et al.*, 2009). Furthermore, human resources are also unequally distributed between the private and public healthcare systems as approximately 70% of the doctors in South Africa are full-time workers in the private healthcare system which provides healthcare to the minority of the population (Van Rensburg, 2004; Mayosi *et al.*, 2014). To try and overcome these inequalities and improve the quality of healthcare in South Africa, National Health Insurance is being proposed.

2.6.2 Costing System used in the Public Healthcare System

Cost studies in the public sector are often limited due to a deficiency of uniform costing information and methodology (Oostenbrink *et al.*, 2002). The public hospitals in South Africa use the *User Guide for the Uniform Patient Fee Schedule* (UPFS) as a common reference for billing patients. The UPFS acts as a simple guide for charging patients in the public hospital as it uses the "grouped fee approach" instead of the "itemised billing approach". Thus, the UPFS has divided most tariffs into the two main categories of facility fee and professional fee (Department of Health, 2009).

The UPFS has stipulated criteria that are used to classify patients as either being: full paying for patients receiving treatment from private HCPs or are funded externally; fully subsidised (H0) for patients that have been referred by Primary Healthcare facilities; or partially subsidised (H1 and H2) patients. The amount of subsidisation for partially subsidised depends on the patient's income and the amount that needs to be paid is calculated as a percentage of the amount charged to patients that are full paying. The UPFS also has free services in which, irrespective of a patient's classification, they do not have to pay for the service. The free services are only for designated circumstances and for patients that fulfil the conditions set out in the UPFS. For example, pregnant women are eligible for free healthcare services but if they are a member of a medical aid scheme, they will be exempt from the free service. It is important to note that that UPFS reflects the fees that the public hospital charges patients and it is not the amount that it costs the hospital to provide patients with healthcare (Department of Health, 2009).

Within the South African public healthcare sector, a medicines tender process is used in which the National Department of Health advertises tenders. Pharmaceutical companies then submit a bid to compete for these tenders and are then awarded the contract for the specified medication at the stipulated price for a period of two years. Therefore each medicine is normally supplied by only one company, or if the tender is split there will be more than one supplier (Gray, 2014). Previously the National Treasury was responsible for the management of medicine tender process, however, this responsibility has now been transferred to the National Department of Health and thus far has been successful in decreasing the cost and increasing the availability of various medicines (Pharasi *et al.*, 2013).

Three sources are predominantly used to finance public healthcare in South Africa. Firstly, the national government distributes its funding amongst provinces using the equitable share formula and thereafter each provincial government decides on the amount to be spent on healthcare. Secondly, conditional grants that are received are once again distributed by the national government to the provincial health departments for use in specified spending areas which includes tertiary hospitals. Thirdly, revenue from each province is also used to pay for public healthcare in that province. Eight programmes are used to categorise provincial health expenditure and expenditure is disturbed differently amongst these programmes as required per province (Day *et al.*, 2015).

2.7 Economic Evaluations of Healthcare Programmes

2.7.1 Economic Evaluations

Economic evaluation can be defined as, “the comparative analysis of alternative courses of action in terms of both their costs and consequences” (Drummond *et al.*, 2005). This definition highlights that the two key components of economic evaluations are costs and consequences and choices. The relationship between costs and consequences of an activity, which is also referred to as inputs and outputs, are used in decision-making. When in a situation where resources are scare, choices have to be made to decide how best to use these scare resources. When deciding whether to allocate scare resources to one activity or another, there are various benefits to performing an economic evaluation. Firstly, economic evaluations require that the current activities are measured and described in order for them to be correctly compared to the new activity as well as to evaluate whether the current activities are cost-effective. Secondly, economic evaluations consider the various viewpoints of a situation, such as the patient, the hospital, or the government. Thirdly, economic evaluations estimate and compare the opportunity cost of the alternative programmes' benefits by measuring the inputs and outputs to determine the value for money achieved (Drummond *et al.*, 2005).

There are various techniques for conducting economic evaluations. The four common ones are Cost-Effectiveness Analysis, Cost-Utility Analysis, Cost-Benefit Analysis and Cost-Minimisation Analysis. The question often arises as to which type of analysis is the best to perform. However, the type of analysis chosen must depend on the situation, the viewpoint of the analyst, as well as other factors (Drummond *et al.*, 2005). Besides conducting the economic evaluation correctly, it is also important to be able to critically analyse the evaluation.

2.7.2 Cost-Analysis

Within all economic evaluations, cost-analyses are essential. When conducting a cost-analysis in a healthcare environment, there are various factors that need to be kept in mind. Irrespective of the type of economic valuation being conducted, the comparative costs are commonly analysed when comparing treatment options or healthcare programmes. It is important to clearly identify the categories and the range of costs to be considered in the study. Thereafter, the quantities of the resources used in each category must be measured and a unit cost or price must be allocated to each category. When calculating costs in healthcare studies, the degree of accuracy and precision of the cost estimates depends on the method used to calculate these costs (Drummond *et al.*, 2005).

When conducting cost-analyses in a healthcare setting using patient data, researchers are faced with different obstacles such as missing data and inconsistency in costing methodology. As missing data is a common problem it is imperative that researchers are aware of the implications of missing data when calculating costs and the alternative methods of how to deal with missing data. When dealing with patient data, uncertainties may arise and there are also various ways to address them using statistical analysis (Drummond *et al.*, 2005).

There are different approached that can be used to calculate costs in healthcare settings: the two common ones are the top-down approach and the bottom-up approach. The top-down approach, also referred to as gross costing or macro-costing, is ideally used in standardised settings and services as the total cost of a setting or service is divided by the number of patients treated by that service to obtain an estimation of the cost. The advantages of the top-down approach is that it is quick and simple to use in hospitals which keep detailed and accessible records of financial and utilization data. However, in hospitals where this data is not available and when settings or services are not standardised, the bottom-up approach should be used. The bottom-up approach, also known as ingredient-based or micro-costing, is when primary data collection is used to obtain information on the utilization of resources

per patient or service in order to calculate the unit cost per patient or service. Although the bottom-up approach may provide more accurate and detailed costs, disadvantages of this approach are that is it time-consuming, costly and the required information may be difficult to obtain. Due to the advantages and disadvantages of both approaches, a mixed approach can be used (Oostenbrink *et al.*, 2002).

There are several different ways to collect patient data for healthcare economic evaluations. Primary data can be collected and used by incorporating the economic evaluation with the randomised control trials for the approval of new products or primary data can be collected by designing new studies specific to economic evaluations of the product. Alternatively, secondary data can be used and analysed in economic evaluations by using decision-analytic modelling. Each method has its own strengths and weaknesses. However, this study focuses on using decision-analytic modelling as a tool to compare the costs and management pathways that follow when using the Conventional Culture Method versus the new Xpert PCR tests for MRSA (Drummond *et al.*, 2005).

2.7.3 Decision-Analytic Modelling

There has been a rise in the use of decision-analytic modelling to conduct economic evaluations to inform decision-making in healthcare settings. As stated by Philips and co-authors (2006), “decision-analytic modelling represents an explicit approach to synthesising currently available evidence regarding the effectiveness and costs of alternative healthcare strategies” in order to aid in decision-making. Decision-analytic modelling has five essential characteristics that fulfil the objectives of economic evaluations. These are structure, evidence, evaluation, uncertainty and variability as well as future research (Drummond *et al.*, 2005).

In situations where there are cases of uncertainty and decisions have to made, decision-analytic models are often used. The two chief components that are common to all types of decision-analytic modelling are probabilities and expected values. When building a decision-analytic model there are a series of steps that need to be followed. Different authors explain and separate these steps in various ways. However, the fundamental concepts are the same and include identifying and defining the decision problem; outlining the boundaries of the model; drawing the structure of the model; identifying and synthesising available data; specifying costs, outcomes and probabilities; conducting calculations and sensitivity analysis; dealing with uncertainty and variability; and applying the models to determine the importance of future research (Drummond *et al.*, 2005; Rascati, 2013).

Unlike other healthcare studies, decision-analytic modelling uses and synthesises data collected from a wide variety of sources such as observations, clinical trials, retrospective patient records, surveys and claim databases (Weinstein *et al.*, 2003). Within the healthcare context, decision-analytic modelling is used in numerous scenarios and is commonly used to compare new treatment alternatives or screening procedures (Werner *et al.*, 2012). In healthcare settings where resources are scarce, such as the South African public healthcare setting, decision-analytic modelling should be frequently conducted to assess which alternatives would be best to implement, thus ensuring the optimal use of available resources.

2.7.4 Economic Evaluations In the South African Healthcare Context

The South African public healthcare setting faces many challenges. Along with its limited resources, there has been an overall increase in the cost of healthcare due to new advances in healthcare, a greater demand for healthcare products and services as well as higher standards of living and expectations. Despite the advantages that are associated with the advances in new pharmaceutical products and diagnostic techniques, they are often associated with a higher price as compared to older alternatives. There is now an increased awareness that decisions have to be made to decide how best to use limited resources, thus economic evaluations are being more frequently conducted in South Africa. With the increase in economic evaluation studies conducted in healthcare settings, it is important that HCPs contribute and cooperate with these studies as well as understand the implications of the outcomes. As established in several countries, South Africa is now also developing formal guidelines for healthcare economic evaluations of new pharmaceutical products (McGee, 2010; Dhamend, 2011). The South African Department of Health published *The Guidelines for Pharmacoeconomic Submissions, December 2012* within the Medicines and Related Substances Act (Act 101 of 1965), under Regulations Relating To a Transparent Pricing System for Medicines and Scheduled Substances. The purpose of this publication is to provide guidelines for transparent and objective economic evaluations to assist decision-making in the South African healthcare context. Although it is aimed at the private healthcare sector in South Africa, these guidelines are also applicable in the public healthcare sector (Department of Health, 2013).

Economic evaluations are also beneficial in situations such as the South African healthcare context in which there is a public healthcare sector as well as where there is a developing National Health Insurance. When deciding on the items to include in the Standard Treatment Guidelines and Essential Drug List as well as in formularies for the public sector, the South African Department of Health is starting to include economic evaluations to guide their decisions. However, economic evaluations are also being used in the private sector in South

Africa due to the increasingly expensive cost of healthcare. The International Society for Pharmacoeconomics and Outcomes Research now also has a South African division, which discusses current health economic issues in respect of the South African context (McGee, 2010). There are also other organizations that address health economics in South Africa such as The Health Economics and Epidemiology Research Office, which is associated with the Wits Health Consortium in Johannesburg and the University of Cape Town's Health Economic Unit.

Although health economic research can provide great value to the South African healthcare system, the quality of health economic research in South Africa is not well established. Thus, Gavaza and co-authors (2012) have conducted a systematic review entitled *The State of Health Economic Research in South Africa*. This review revealed that health economic research relating to South Africa was of fair or poor quality in contrast to a higher quality found in the health economic research relating to South Africa that was published overseas. This demonstrates that South Africa needs to improve the quality of health economic research conducted in order for such research to portray its true benefits. However, Gow and co-authors (2013), who are health economic researchers, have analysed and highlighted certain points of this systematic review such as that the title and the contents are misleading as they are not a completely objective review of the current economic situation in South Africa due to various reasons including that key South African researchers and economic organizations in the field have been omitted. It is commonly accepted, however, that there is a pressing need for further costing and health economic studies in the South African context to further inform decision-making.

2.8 Building Decision-Tree-Analytic Models to Compare the Conventional Culture Method and PCR Testing for MRSA

As decision-analytic modelling is a useful tool for assessing alternatives, studies have developed decision-analytic models to compare the costs of using the Conventional Culture Method versus the new PCR testing for MRSA (Li *et al.*, 2012; Tübbicke *et al.*, 2012a).

With the introduction of the Xpert MRSA tests at a University Hospital in Norway, Li and co-authors conducted a study to compare and calculate the cost-effectiveness of the new Xpert MRSA tests to the currently used culture tests by developing a decision-tree-analytic model in TreeAge. In addition, this study looked at two different strategies of the Xpert MRSA tests: the daytime strategy and the 24-hour strategy. The information for the model was obtained by conducting an actual trial study in the hospital on inpatients that were at a high risk of MRSA infection. It was found that overall not only were the Xpert MRSA tests less expensive

than the culture tests, but the Xpert tests were associated with additional positive outcomes such as decreased time of pre-emptive isolation (Li *et al.*, 2012).

The results found by Li and co-authors are in line with the results found by other studies that also developed decision-tree-analytic models. Although some of these studies used different types of information and measured different outcomes in their models, the results showed that the Xpert MRSA tests are preferred. A study conducted by Brown and Paladino, which developed a decision-tree-analytic model on TreeAge to assess the effects of using PCR tests, using information mainly from peer-reviewed literature, found the Xpert MRSA to be less expensive than the current strategies as well as possibly decreasing mortality rates in the European Union and the United Sates. (Brown *et al.*, 2010).

However, decision-tree-analytic models comparing the costs and management pathways that follow when testing for MRSA have not yet been built for the South African healthcare context. It is important that these studies are conducted and models are developed in relation to healthcare in South Africa due the country's socio-economic status and access to healthcare being different as compared to other countries (Ataguba *et al.*, 2011)**.** Once these models are built, they can be used in different situations to compare MRSA diagnostic alternatives to aid in decision-making in South African hospitals.

3. METHODOLOGY

3.1 Theoretical Framework

This study aimed at conducting a cost-analysis to investigate the management pathways and associated costs of the current Conventional Culture Method versus new PCR testing for MRSA. However, from the outset of this study, it was found that research on this topic has not yet been conducted in the South African public healthcare context, nor was much information from the South African public healthcare context available on the separate aspects of this study. Therefore it was necessary for qualitative research to first be conducted to provide a background of the current practices in the chosen setting. The information acquired from the qualitative research guided and informed the quantitative research aspects of this study.

The perspective used in this study was that of the South African public healthcare sector. Only the direct costs and utilization of antibiotics and laboratory tests that isolated MRSA in the study population were analysed in this study. All costs in this study are expressed in South African Rands (R).

3.2 Study Design

A mixed method research design was selected for this study as it consisted of both qualitative and quantitative methods to comprehensively answer the research question. Qualitative observations were conducted to provide an understanding of the current daily practices of HCPs in order to assist the collection and interpretation of retrospective patient records as well as to provide a more realistic approach when performing the cost analysis and developing the decision-tree-analytic models reflecting the patient management pathways.

There are various methods in which qualitative and quantitative research could be conducted. In this study, Ethnography was chosen as the qualitative research method and Inductive Analysis was used to analyse the data collected. As this study did not include implementation of an intervention, it was a non-experimental study and thus the quantitative methods chosen were a secondary data analysis for the Retrospective Records Review and an economic evaluation for the Cost Analysis and Decision-Tree-Analytic Models.

This study consisted of four methods. The first method involved conducting qualitative observations in the chosen hospital wards, the NHLS Microbiology Laboratory and the antibiotics section of the main dispensary at the CMJAH. The remaining three methods were quantitative and included a Retrospective Patient Records and Antibiotic Utilization Review,

a Costs Analysis and developing Decision-Tree-Analytic Models. Thus there was greater emphasis on the quantitative section of this study. Figure 1 represents the study design. The detailed study methodology will be further explained in Section 3.7 and 3.8.

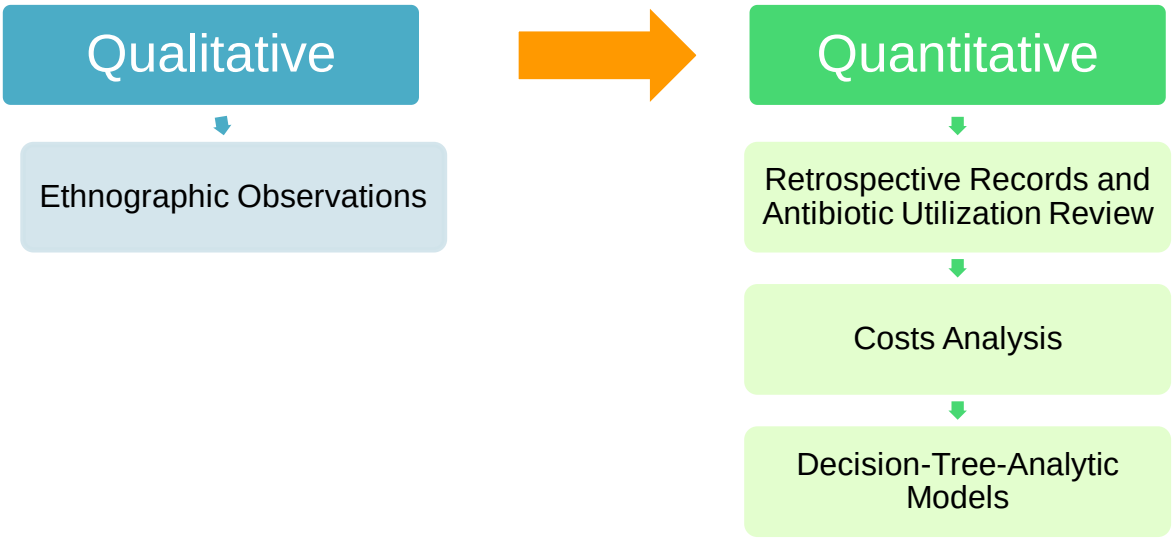


Figure 1: Study Design Showing Mixed Methods Research: Qualitative Methods used to Inform Quantitative Methods

3.3 Study Site

This study was conducted at CMJAH in Johannesburg, South Africa. CMJAH is a public sector hospital that provides secondary, tertiary and highly specialised services.

Within the CMJAH the study sites included:

- The Orthopaedic Ward
- The Vascular Ward
- The NHLS Microbiology Laboratory
- The Hospital's Medical Records Room
- The Antibiotics Designated Area of the Main Dispensary

3.4 Study Population

To determine the study population, an application was submitted to the NHLS Information Systems to request details of all the patients at CMJAH that had been identified as MRSA-positive in 2013. From the data received from the NHLS Information Systems, there were 702 samples that were MRSA-positive at CMJAH in 2013. These 702 samples were taken from 373 patients. The information received from the NHLS information system was sorted and filtered to reveal the wards that had the highest number of patients with MRSA during 2013 as shown in Table 1.

Table 1: Number of Microbiology Laboratory Tests and Number of Patients that Isolated MRSA per Ward at CMJAH in 2013

Number of Laboratory Tests	Number of Patients	Type of Ward
104	42	Paediatric Surgery and Trauma
60	25	Trauma ICU / Surgery
57	36	Vascular
49	36	Trauma Surgery
47	18	Orthopaedic
42	24	General ICU

General Trauma and ICU wards were excluded due to the wide range of conditions affecting the patients in these wards thus making it difficult to follow treatment care pathways as well as due to the high turn-over of patients in these wards. The paediatric ward was also excluded as paediatric care differs from adult care and thus it would not be consistent for comparison purposes. Therefore, the study population consisted of inpatients that were diagnosed with MRSA in 2013 in the orthopaedic ward and the vascular ward at CMJAH as shown in Figure 2.

A convenience sample was used in this study. The data received from the NHLS Information Systems contained the patient's hospital number, ward number and other patient details as well as information about the laboratory tests of the patients that had MRSA in 2013. The data was filtered to find all the patients that were in the vascular and orthopaedic wards. The patient numbers of these patients were then used to access their retrospective medical records from the Hospital's Medical Record Room. When accessing the retrospective patient records, patients whose records could not be found or did not contain 2013 information were excluded.

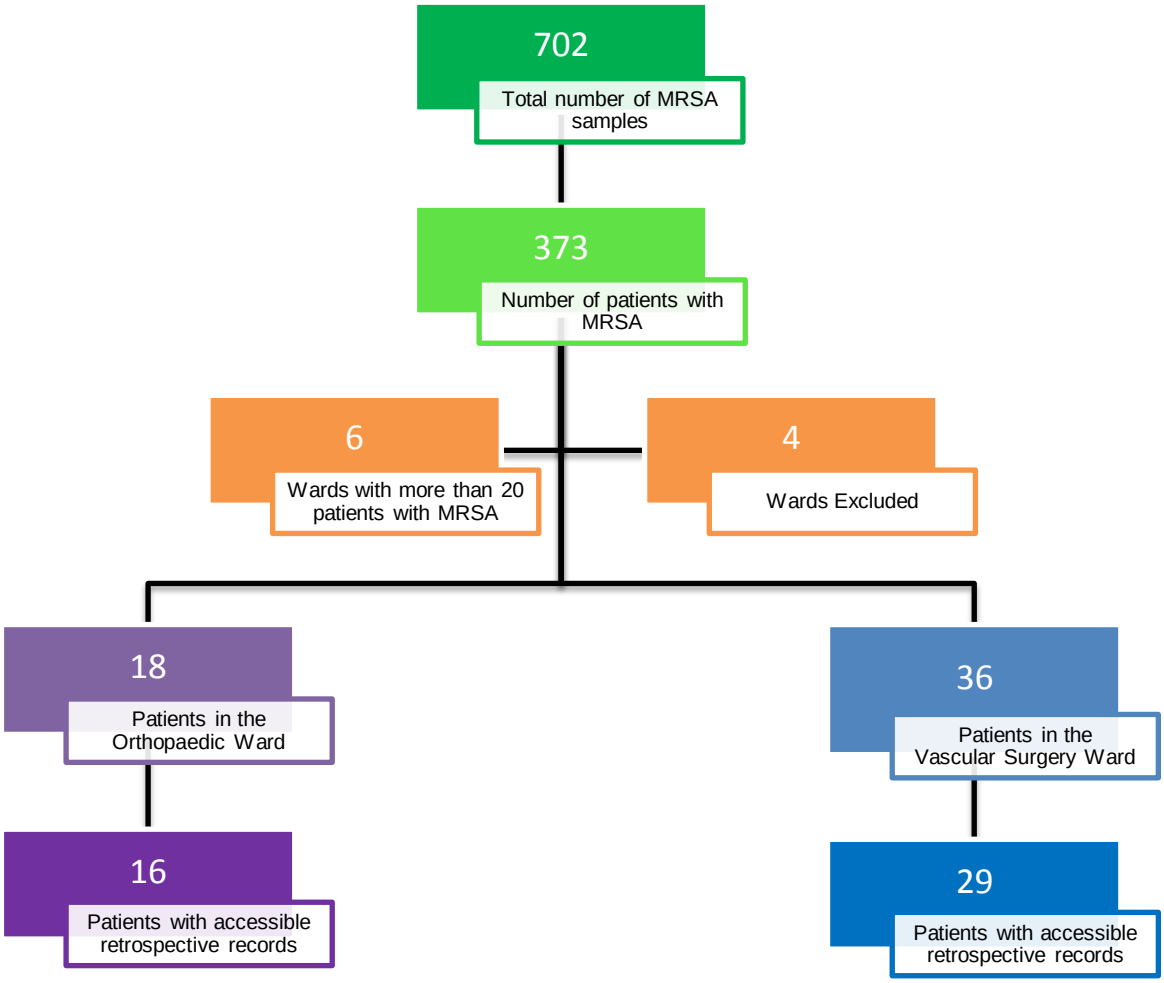


Figure 2: Breakdown of the Number of Samples and Patients that Isolated MRSA at CMJAH in 2013 to Determine the Study Population

3.5 Study Duration

The study was conducted between January 2013 and January 2015.

Observations of clinical practice were conducted in the following areas:

- Orthopaedic Ward during November 2013
- Vascular Ward during April 2014
- NHLS Microbiology Laboratory during February 2014
- Antibiotics designated area of the main dispensary at CMJAH during September 2014

Data was collected from the Hospital's Medical Records Room:

- For the patients in the Orthopaedic Ward during February 2014 to March 2014
- For the patients in the Vascular Ward during May 2014 to June 2014

3.6 Ethical Considerations

An application was submitted to the Human Research Ethics Committee: (Medical) for Clearance of Research and ethical clearance for this study was approved in 2013 (M130543).

Written permission was then requested and granted from the CEO of CMJAH, Ms Bogoshi. Permission was also obtained from Professor Lukhele (head of the orthopaedic ward), Professor Veller (head of the vascular ward) and Dr Bosman from NHLS, as well as the Hospital's Medical Records Room and the Responsible Pharmacist of the Dispensary at CMJAH.

The Ethics Clearance Certificate and Letter of Research Permission for this study are in Appendix 1 and Appendix 2 respectively.

3.7 Data Collection Procedures

The data for this study was collected using four methodologies, the first being Qualitative Observation of Clinical Practice and the remaining three were Quantitative Retrospective Records Review, Cost Analysis and Decision-Tree-Analytic Models.

3.7.1 Ethnographic Observations

Ethnography includes conducting observations to obtain the required information by concentrating on the details to produce a thorough narrative account and understanding. Inductive Analysis is a systematic procedure in which the specific data collected is arranged into segments, codes and categories and then general patterns were recognised. A data segment is a single idea that can be understood on its own; these segments are then labelled by one or more codes. Similar codes are then grouped into categories depicting the main ideas of the data and the relationship between the categories are then described by patterns (McMillan *et al.*, 2014).

A special feature of ethnographic observations is that they are conducted within the natural setting of the study population, thus allowing for natural daily behaviour to be observed and documented (Reeves *et al.*, 2008). This study used the stance of non-participant observations, in which the observer was a complete outsider who did not participate in the practices being observed nor offer any contribution to ensure the reliability and validity of the observations. This method consisted of ethnographic observations of the daily practices of HCPs at CMJAH.

3.7.1.1 Data Collection by Ethnographic Observations

Ethnographic observations were used as a tool to gain an understanding of the naturally occurring practices at the study site and to ensure that the data collected included all the essential information (Reeves *et al.*, 2008). It was not possible to collect all of the required information from the ethnographic observations that were performed, such as information regarding the criteria followed for placing a patient in isolation. Thus, HCPs involved in patient care in the current setting were approached to clarify issues verbally when more detail concerning policies or practices was required.

Ethnographic observations were conducted in the orthopaedic and vascular wards as well as at the NHLS Microbiology Laboratory and the main dispensary at CMJAH. The general methodology for the ethnographic observations conducted is explained below. Thereafter, under the subsequent headings the specific methodology for the ethnographic observations conducted in each area is outlined.

Once the study site was selected and permission in each of the study areas was obtained, general observations were first conducted to become familiar with the activities. This was followed by observations to document the details of the activities specific to the areas. During observations in the various areas, details were recorded regarding the general aspects of who was involved in the activities; what type of activities occurred; where and when the activity took place; and why the HCPs interacted in the observed manner. The specific factors that were observed and documented for each area are described in the following sections.

The data obtained from the observations were documented as field notes and reflex records which were then analysed in the results section. Field notes contained the date, setting and data that were collected during the observations; reflex records were the notes written immediately after the observations to interpret the main activities and assess the data collected to identify information that was missing.

3.7.1.1.1 Clinical Ward Observations

Observations were conducted in the two wards to understand the clinical practices of HCPs regarding the current management of patients suspected of having an MRSA infection and the clinical pathways that followed, depending on whether the patient had MRSA or not. The purpose of the observations was to get a clear picture of what actually happens in daily practice. This was essential to ensure that appropriate data was collected for the CMJAH setting and to assist in understanding and interpreting the patient records when looking at the retrospective patient records.

The observations were conducted during the doctors' early morning ward rounds over seven days in each ward. Each observation lasted for the duration of the ward round (approximately 30 minutes per ward). The observations did not interfere or have any impact on the ward rounds.

During the observations in the wards, information was obtained and details were documented in the 8.3.1 Clinical Ward Observation Data Collection **Sheet** shown in Appendix 3. Particular attention was observed and documented for the following:

- Doctor-Patient interaction
- The use of antiseptic/disinfectant hand rub and hand washing
- The use of Personal Protective Equipment (PPE)
- Prescribing of antibiotics for suspected and confirmed infection
- Request for and taking of specimens to be sent to the NHLS Microbiology Laboratory for suspected infections
- Action taken while waiting for the patients results from the NHLS Microbiology Laboratory
- Pre-operative, post-operative and wound care
- Criteria and method of isolation of patients with suspected and confirmed infection

3.7.1.1.2 NHLS Microbiology Laboratory Observations

Observations were conducted in the NHLS Microbiology Laboratory at CMJAH to understand the current method of testing for a suspected MRSA infection. Observations were conducted at the bacteriology bench (“bact-bench”) in the microbiology laboratory. The purpose of the observation was to understand the current methods and get a clear picture of what happens in daily practice. This was essential to ensure that appropriate data was collected for the CMJAH setting and to assist in understanding and interpreting the patient records when looking at the retrospective patient records.

The observations were conducted during the morning shift over five days. Each observation lasted for the duration of the first morning shift (time varied depending on the number of samples received each morning). The observations did not interfere or have any impact on the shift.

During the observations in the microbiology laboratory, information was obtained and details were documented in the 8.3.2 Microbiology Laboratory Observation Data Collection Sheet presented in Appendix 3. Particular attention was observed and documented for the following:

- The procedure from when a specimen for a suspected infection is received until a confirmed diagnosis is made.

- The steps involved during the different stages of Microscopy, Culture and Sensitivity.
- The time taken and laboratory personnel involved in performing each of these steps.
- Special attention was observed for the steps and procedure involved when a Gram-positive *Staphylococcus aureus* and MRSA infection was suspected and detected in the laboratory.

3.7.1.1.3 Antibiotic Dispensary Observations

Information regarding the current antibiotic dispensing policies for inpatients at CMJAH was obtained from the antibiotics designated section of the dispensary at CMJAH. The information was obtained by basic observations and the pharmacist assisted by providing further information required to complete the field notes. The information obtained was recorded in the 8.3.3 Antibiotic Dispensary Observation Data Collection Sheet shown in Appendix 3.

Particular information required regarding the common Empiric and MRSA-Specific Antibiotics used in each ward was:

- The general policy used for dispensing antibiotics to inpatients.
- Policy for antibiotics kept in ward stock versus antibiotics dispensed on a per-patient basis.
- The antibiotics which require authorisation from consultants.
- The antibiotics which require confirmation of infection from NHLS sensitivity results.
- Additional policy for dispensing vancomycin, linezolid and carbapenems.
- Current Antibiotic Stewardship practice in the hospital and dispensary.

3.7.2 Retrospective Records and Antibiotic Utilization Review

A retrospective records review was conducted by accessing the medical records of the patients in the study population from the Medical Records Room at CMJAH.

3.7.2.1 Data Extraction Procedure

The Hospital's Medical Records Room has a manual system for storing and accessing patient records. However, the manual system is slowly being replaced by an electronic computerised system. The system used to retrieve the records was as follows:

- The last digit of a patient's hospital number was used as an indication of which area in the room to look. Example: all records ending in 0 were kept opposite the entrance of the room. Next to that were all records ending in 1 and so forth.
- Once the area in the room was located, the mini filing drawers were labelled with the range of patient numbers that were within the drawer.
- Within each drawer there were brown envelopes arranged in numerical order, each envelope had a hospital number on the front and was for an individual patient.

- Each envelope contained microfiche films of the individual's patient records.
- A place holder was put in the place of the required patient number and the envelope was removed.
- The microfilms were viewed through the microfiche viewer.
- All patient records since June 2013 for patient numbers ending in 6, 7, 8 and 9 were on the electronic computer system.
- These records were accessed by typing the patient's hospital number into the computer program and the required document was opened as a PDF of the scanned patient records.

Before extracting and recording data from the patients' retrospective records, patient numbers (For example 369P01, 369P02) were allocated to each patient's hospital number. The links between the allocated patient number and the patient's hospital number were stored separately in a password-protected file. Therefore, when recording a patient's information on a case report form, the allocated patient number was used and the patient's actual hospital number, name, surname or any other patient-identifying data was not recorded. This was done in accordance with the ethics application in order to maintain patient confidentiality and anonymity.

Patient records are not permitted to be photocopied, printed or transcribed directly onto a laptop, so all required information had to be handwritten in the Records Room and then transcribed in Excel spread sheets once outside the Records Room.

3.7.2.2 Collection of Retrospective Patient Data

Data was extracted from patient records and then recorded on individual patient case report forms, as in Appendix 4. Specific data that was extracted from the retrospective records was:

- Age
- Gender
- Date of Admission
- Date of Discharge
- Diagnosis / ICD10 Codes
- Operations and surgical procedures
- Doctors notes regarding infection control; isolation; samples taken and sent for MCS for suspected infection; laboratory test information for suspected infections; antibiotics prescribed, administered, changed, or doses adjusted
- NHLS laboratory results relating to infections
- Antibiotic information (name, strength, dose, route, duration) on doctors' prescription charts and nurses' administration charts

The data that was recorded on the individual patient case report forms was then entered into an Excel template created per ward. When entering the patients' data collected from the retrospective records, there was missing information. Some of the missing information was obtained by consulting with various HCPs from the wards, the laboratory personnel at the NHLS Microbiology Laboratory and the pharmacist at the antibiotics designated area of the dispensary as well as by making assumptions which are stated in Section 5.9.

3.7.3 Cost Analysis

The costing methodology used in this study was the bottom-up approach. This approach was used as official databases containing the specific utilization and costing information were not found at CMJAH. Furthermore, although MRSA laboratory test utilization and costing information was obtained from the NHLS Information Systems, based on the observation at the wards, standardisation of clinical practice could not be deduced. Therefore, prior to performing the cost-analysis, primary data collection was conducted to obtain the utilization information of the antibiotics administered and MRSA laboratory tests conducted in the study population.

3.7.3.1 Costing Information

The antibiotic, NHLS laboratory test and Xpert MRSA costing information was obtained and filtered according to the utilization data collected from the retrospective patient records. The summarised databases formulated and used are in Appendix 5.

3.7.3.1.1 Antibiotic Costing Information

The costing information for the antibiotics was taken from the "Database Medsas-contract-prices-INN-ATC 2013". This was a 2013 database for the cost of antibiotics in public hospitals in South Africa. A list of all the antibiotics used in the study population was formulated for each ward and was allocated its respective cost from the database as shown in Appendix 5 (Table 29 and Table 30). These summarised databases were used when conducting the antibiotic cost calculations; the Average weighted price (contract) was used but when this was not available the Depot price Mar-13 (without mark-up) was used.

3.7.3.1.2 NHLS Laboratory Test Costing Information

The costing information for the NHLS laboratory tests that isolated MRSA was obtained from the costing information requested and received from the NHLS Information System. The costing data was then filtered to formulate a list of the different steps used in the laboratory tests that were conducted to detect MRSA in the study population for each ward. A list of the laboratory tests that isolated MRSA for each patient was then formulated for each ward and the respective costs were allocated to each test as listed in Appendix 5 (Table 31 and Table

32). These summarised databases were used when conducting the NHLS laboratory tests cost calculations.

3.7.3.1.3 Xpert MRSA Costing information

The price of the Xpert PCR kits for MRSA was obtained from a quote requested and received from Cepheid South Africa in May 2014 (QT1005SP). The information from the quote is summarised in Appendix 5 (Table 33).

3.7.4 Decision-Tree-Analytic Models

Decision-tree-analytic models were developed using TreeAge Pro 2013 Software and the TreeAge Pro 2013 User's Manual (TreeAge Software INC, 2013). The decision-tree-analytic models were populated with input parameters from the observations, retrospective records, cost analysis, experts' opinions and the published literature. The plausibility of the models was assessed by varying the probabilities and costs of inputs for each branch (including the potential cost of the Xpert MRSA test). TreeAge Rankings, Sensitivity Analysis and Tornado Analysis were then performed to determine which pathway was most efficient and which variables were most sensitive.

3.7.4.1 Patient Management Pathways

Using the information obtained from the observations and retrospective records review, the various management pathways of a patient with a suspected infection were formulated as branches of a decision-tree-analytic model.

A management pathway was formulated for each patient with a suspected MRSA infection to show the clinical pathways that followed regarding the administering of antibiotics and the collection of specimens for MCS as well as the steps taken while waiting for the laboratory test results and after the results were available. The management pathways were then grouped and used to formulate an 'actual' clinical decision-tree-analytic model per ward. Based on the clinical decision-tree-analytic models, a theoretical arm was added to the actual decision-tree-analytic model to represent possible scenarios of implementing the Xpert MRSA PCR tests.

Each model started at the decision node with a patient with a suspected MRSA infection. The first set of branches after the decision node represents the various strategies used to manage patients with a suspected infection. The branches after the chance node represent the options within each strategy.

3.7.4.2 Decision-Tree-Analytic Model Structure

For each ward a decision-tree-analytic model was developed to describe the current management of patients with a suspected and confirmed MRSA infection.

Using the structure of the actual decision-tree-analytic model developed for each ward, a fourth arm was then added to evaluate effects and the clinical pathway that would follow if the Xpert MRSA PCR tests were to be implemented in the current clinical settings. The variable cost of the Xpert MRSA test was calculated from the quote received from Cepheid South Africa.

3.7.4.2.1 Decision-Tree-Analytic Model Structure for the Orthopaedic Ward

When a patient presented with a suspected infection in the orthopaedic ward, represented at the decision node, there was a range of clinical practices that could have been carried out as illustrated in Figure 3 and explained below. The branches from the decision node represent the alternative clinical practices that were performed for a patient that had a suspected infection: A patient would either first receive Empiric Antibiotics to try and treat the infection (first top branch); or a patient would have a specimen taken and sent for MCS to investigate the source of the infection (second branch); or a patient would have a specimen taken and sent for MCS and receive Empiric Antibiotics while waiting for the MCS results (third branch). The possible pathway that would follow if the Xpert MRSA test were to be implemented in the current clinical setting was represented by the fourth bottom branch.

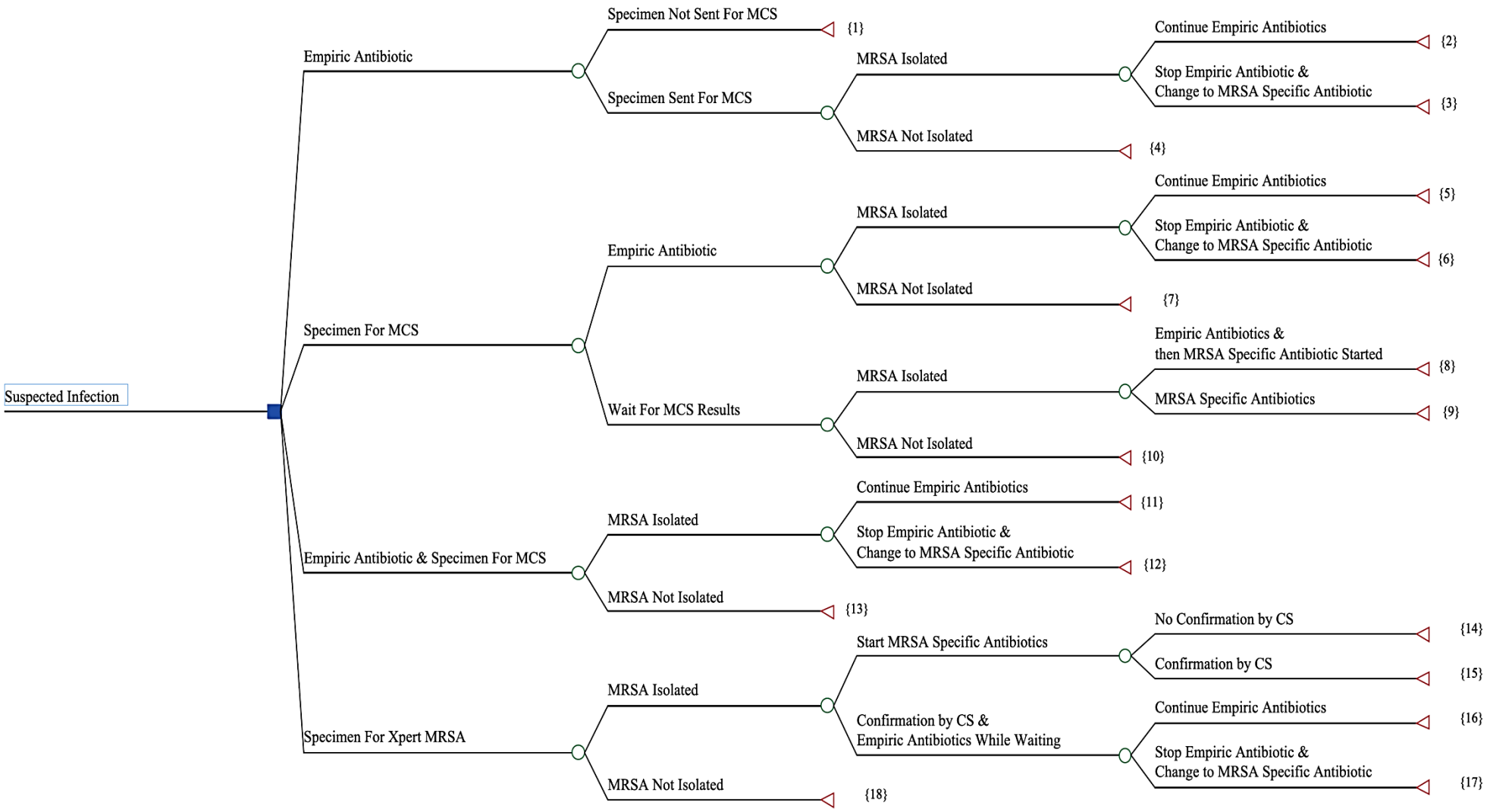


Figure 3: Decision-Tree-Analytic Model Structure Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward

Each of the four branches Figure 3 ends with chance nodes representing possible outcomes. The branches from the chance node either ended with another chance node representing further possible outcomes, or ended with a terminal node representing the endpoint, which has no further branches. Payoffs were assigned to the terminal node, representing the net value of that pathway.

The first branch describes the pathway taken if a patient first received Empiric Antibiotics once an infection was suspected. Once the patient received the Empiric Antibiotics the first chance node describes the possible outcomes that either the patient had a specimen sent for MCS or that the patient did not have a specimen sent for MCS to investigate the source of infection. If the patient did not have a specimen sent for MCS, a terminal node and a payoff were assigned to that branch. If the patient had a specimen sent for MCS, a second chance node was added to that branch with the possible outcome of MRSA isolated or MRSA not isolated. If MRSA was not isolated, a terminal node and a payoff were assigned to that branch. If MRSA was isolated, a third chance node was assigned with the possible outcomes of either continue Empiric Antibiotics or Empiric Antibiotics stopped and changed to MRSA-Specific Antibiotics. Both of these outcome branches were assigned terminal nodes and payoffs.

The second branch describes the pathway taken if a specimen was first sent for MCS when an infection was suspected. Once a specimen was sent for MCS, there were two possible outcomes that were represented by a chance node. Either to start Empiric Antibiotics while waiting for the MCS results or to wait for the MCS results without starting Empiric Antibiotics. If Empiric Antibiotics were started while waiting for the MCS results, a second chance node was added to the branch with the outcomes of MRSA isolated or MRSA not isolated. If MRSA was not isolated, a terminal node and a payoff were assigned to that branch. If MRSA was isolated, a third chance node was assigned with the possible outcomes of either Empiric Antibiotics continued or Empiric Antibiotics stopped and changed to MRSA-Specific Antibiotics. Both of these outcome branches were assigned terminal nodes and payoffs. However, if after a specimen was sent for MCS, the outcome was to wait for the results, a chance node was added to this branch with the possible outcomes of MRSA isolated or MRSA not isolated. If MRSA was not isolated, a terminal node and a payoff were assigned to that branch. If MRSA was isolated, a third chance node was assigned with the possible outcomes of either MRSA-Specific Antibiotics administered or first Empiric Antibiotics and then MRSA-Specific Antibiotics administered. Both of these outcome branches were assigned terminal nodes and payoffs.

The third branch describes the pathway for when a Specimen For MCS was taken and at the same time Empiric Antibiotics were administered when an infection was suspected. The first chance node had the possible outcome of either MRSA isolated or MRSA not isolated. If MRSA was not isolated a terminal node and payoff were assigned to that branch. If MRSA was isolated a second chance node was allocated to that branch with the possible outcomes of either to continue Empiric Antibiotics or to stop Empiric Antibiotics and change to MRSA-Specific Antibiotics. Both of these outcome branches were assigned terminal nodes and payoffs.

The fourth branch represents the scenario of implementing the Xpert MRSA test in the current clinical setting which was to send a Specimen For Xpert MRSA testing when an infection was suspected. This branch ended with a chance node with the possible outcomes of MRSA isolated or MRSA not isolated. The branch of MRSA not isolated ended with a terminal node and a payoff. The branch of MRSA isolated ended with a chance node with two possible outcomes of either to immediately start MRSA-Specific Antibiotics or to first confirm the MRSA result by a culture and sensitivity test and administer Empiric Antibiotic while waiting for the culture and sensitivity results. The branch of start with MRSA-Specific Antibiotics ended with a chance node with the outcome of either to confirm the Xpert MRSA result by a culture and sensitivity test or not to confirm by a culture and sensitivity test. These two branches ended with a terminal node and a payoff. The alternative branch of to first confirm by culture and sensitivity tests and administer Empiric Antibiotics while waiting also ends with a chance node with the possible outcomes of continue Empiric Antibiotics or stop Empiric Antibiotics and start MRSA-Specific Antibiotics once the culture and sensitivity test results were available. These two branches ended with a terminal node and a payoff.

3.7.4.2.2 Decision-Tree-Analytic Model Structure for the Vascular Ward

When there was a patient with a suspected infection in the vascular ward, the branches from the decision node were the same as the branches from the decision node in the clinical practice decision-tree-analytic model Structure for the orthopaedic ward: First Branch of Empiric Antibiotics, Second Branch of Specimen For MCS and Third Branch of Empiric Antibiotic & Specimen For MCS. The possible pathway that would follow if the Xpert MRSA test were to be implemented in the current clinical setting was represented by the fourth bottom branch. The possible outcome branches from the chance nodes were slightly different as illustrated in Figure 4 and explained below.

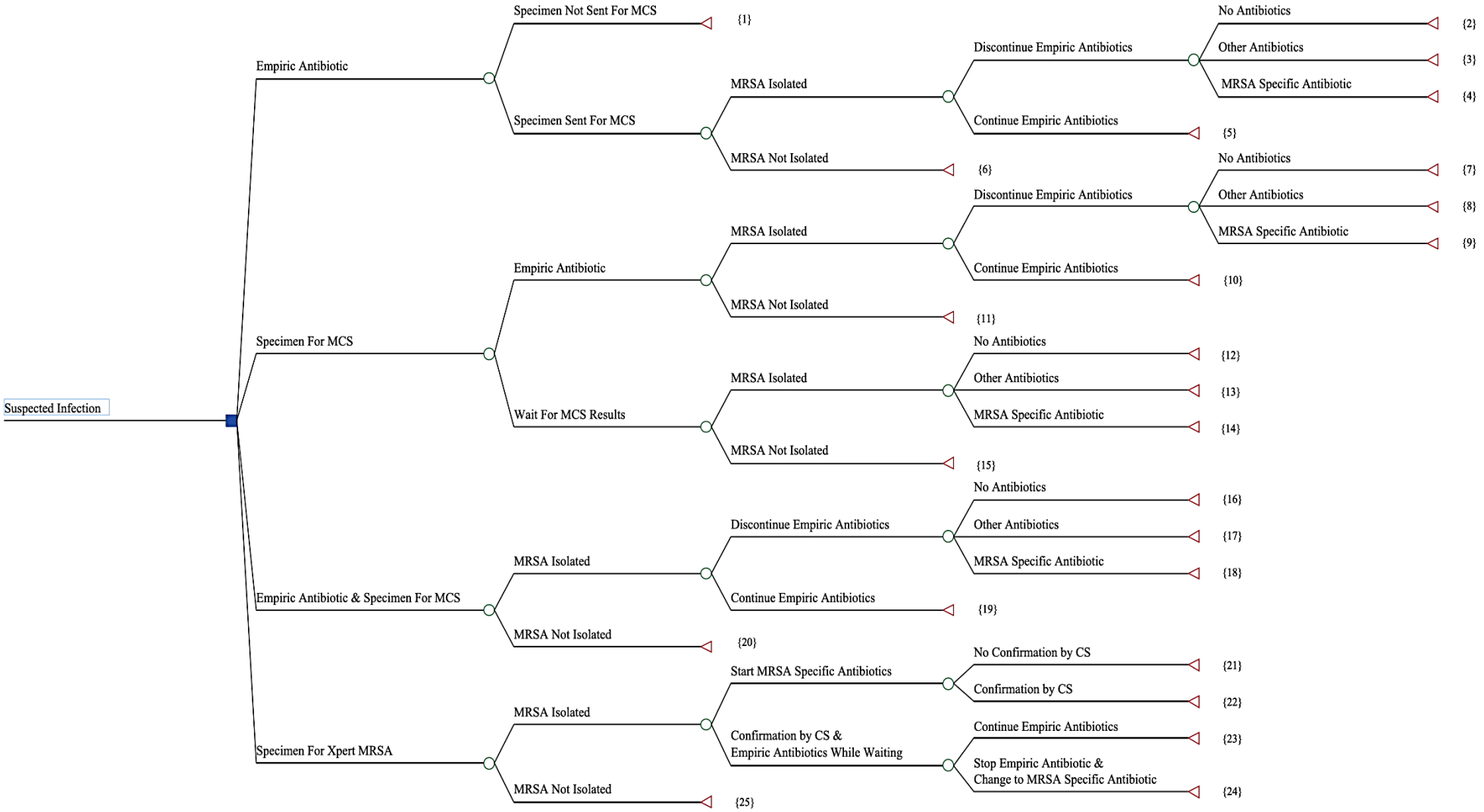


Figure 4: Decision-Tree Analytic Model Structure Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward

The first branch from the decision node describes the pathway of first administering Empiric Antibiotics to a patient with a suspected infection. This branch ended with a chance node with the possible outcomes of sending a Specimen For MCS or not sending a Specimen For MCS to investigate the source of infection. If a specimen was not sent for MCS, the branch ended with a terminal node and was allocated a payoff. If a specimen was sent for MCS, the branch ended with a chance node with the possible outcomes of MRSA isolated or MRSA not isolated. If MRSA was not isolated the branch ended with a terminal node and a payoff. If MRSA was isolated, the branch ended with a chance node with the possible outcomes of discontinuing Empiric Antibiotics or continuing Empiric Antibiotics. The discontinuing Empiric Antibiotics branch ended with a chance node with the possible outcomes of No Antibiotics, Other Antibiotics, or MRSA-Specific Antibiotics administered. These three branches all ended with a terminal node and a payoff. The branch continuing with Empiric Antibiotics also ended with a terminal node and a payoff.

The second branch from the decision node describes the pathway of first sending a Specimen For MCS when a patient had a suspected infection. This branch ended with a chance node with the possible outcomes of starting Empiric Antibiotics while waiting for the MCS results or to wait for the MCS results without starting Empiric Antibiotics. If Empiric Antibiotics were started while waiting for the MCS results, a second chance node was added to the branch with the outcomes of MRSA isolated or MRSA not isolated. If MRSA was not isolated, a terminal node and a payoff were assigned to that branch. If MRSA was isolated, a third chance node was assigned with the possible outcomes of discontinuing Empiric Antibiotics or continuing Empiric Antibiotics. The discontinuing Empiric Antibiotics branch ended with a fourth chance node with the possible outcomes of No Antibiotics, Other Antibiotics, or MRSA-Specific Antibiotics administered. These three branches all ended with a terminal node and a payoff. The branch continuing Empiric Antibiotics also ended with a terminal node and a payoff. However, if after a specimen was sent for MCS, the outcome was to wait for the results without receiving Empiric Antibiotics, a chance node was added to this branch with the possible outcomes of MRSA isolated or MRSA not isolated. If MRSA was not isolated, a terminal node and a payoff were assigned to that branch. If MRSA was isolated, another chance node was assigned with the possible outcomes of discontinuing Empiric Antibiotics or continuing Empiric Antibiotics. The discontinuing Empiric Antibiotics branch ended with a chance node with the possible outcomes of No Antibiotics, Other Antibiotics or MRSA-Specific Antibiotics administered. These three branches all ended with a terminal node and a payoff. The branch continuing Empiric Antibiotics also ended with a terminal node and a payoff.

The third branch from the decision node describes the pathway for when a Specimen For MCS was taken and at the same time Empiric Antibiotics were administered when an infection was suspected. The first chance node had the possible outcome of either MRSA isolated or MRSA not isolated. If MRSA was not isolated a terminal node and a payoff were assigned to that branch. If MRSA was isolated a second chance node was allocated to that branch with the possible outcomes of discontinuing Empiric Antibiotics or continuing Empiric Antibiotics. The discontinuing Empiric Antibiotics branch ended with a third chance node with the possible outcomes of No Antibiotics, Other Antibiotics or MRSA-Specific Antibiotics administered. These three branches all ended with a terminal node and a payoff. The branch continuing Empiric Antibiotics also ended with a terminal node and a payoff.

The fourth branch was to send a Specimen For Xpert MRSA testing when an infection was suspected. This branch ended with a chance node with the possible outcomes of MRSA isolated or MRSA not isolated. The branch of MRSA not isolated ended with a terminal node and a payoff. The branch of MRSA isolated ended with a chance node with two possible outcomes of either to immediately start MRSA-Specific Antibiotics or to first confirm the MRSA result by a culture and sensitivity test and administer Empiric Antibiotics while waiting for the culture and sensitivity test results. The branch of starting with MRSA-Specific Antibiotics ended with a chance node with the outcome of either confirming by culture and sensitivity tests or not confirming by culture and sensitivity tests. These two branches ended with a terminal node and a payoff. The alternative branch of first confirming by culture and sensitivity tests and administering Empiric Antibiotics while waiting also ended with a chance node with the possible outcomes of continuing Empiric Antibiotics or stopping Empiric Antibiotics and starting MRSA-Specific Antibiotics once the culture and sensitivity test results were available. These two branches ended with a terminal node and a payoff.

3.7.4.3 Decision-Tree-Analytic Model Parameters

Once the structure Decision-Tree-Analytic Models were complete, the respective parameters were calculated and entered into the models. The variable costs for these models were derived from the cost-utilization calculations conducted per ward. The probabilities entered for the actual models were based on the data collected from the retrospective records of the patients in the study population

3.7.4.3.1 Variables

Variables are parameters that are allocated to the branches of the tree. They contain the numeric value for the parameter as well as the high and low values for the parameter, which are used for sensitivity analysis. The numeric values for the parameters were obtained from the cost calculations conducted. The costs entered for the Antibiotic variables

(cDailyEmpiricAntibiotic, cDailyMrsaSpecificAntibiotic and cDailyOtherAntibiotic) were the average of the daily antibiotic cost per ward. The costs entered for the NHLS laboratory test variables (cSpecimenM and cSpecimenCS) were the average of the NHLS laboratory test cost per ward. For each antibiotic variable the standard deviation of the daily antibiotic cost per ward was calculated and added to the average cost to calculate the high value and subtracted from the average to calculate the low value. For the NHLS laboratory test variables, the standard deviation of the NHLS laboratory test cost per ward was also calculated and used to obtain the high and low values. When a negative value was obtained, zero was entered for the low value.

For the cXpertMRSA variable, the average cost of one Xpert MRSA test was used and 50% was added to the cost for the high value and 50% was subtracted from the cost for the low value.

For the theoretical situation that was run using variables to represent equal probabilities for each branch in the model, the numeric value for the probability variables created was either 0.5 or 0.33 depending on the number of branches present when allocating the probability. To obtain the high values and low values for the probability variables, 50% was added and 50% was subtracted from the numeric value of the variable (i.e. 0.5 or 0.33).

3.7.4.3.2 Probabilities

The probability of a patient following a certain pathway was then added to the models. Probabilities were assigned to every branch that came out from a chance node. On the models, the probability of an outcome was represented by the number below its respective branch. The sum of the branch probabilities from a chance node was equal to one.

The probabilities for the actual models were derived from the information obtained from the patients' retrospective records. For the theoretical arm introducing the Xpert MRSA, the sub-trees that were the same as the clinical arms had the same probabilities as the clinical arms and the sub-trees that represented the theoretical situation were assigned equal probabilities of 0.5 when there were two branches and 0.33 when there were three branches emanating from a chance node.

The actual decision-tree-analytic models were then run by creating and using variables to allocate equal probabilities to each branch of the model for each ward. These were then referred to as the equal decision-tree-analytic models. For these models, it was assumed that a patient had an equal chance of experiencing either outcome, thus equal probabilities were allocated to each branch (0.50 when there were two branches and 0.33 when there

were three branches). For these models, instead of using numeric values, variables were created and used as the probabilities for each branch.

3.7.4.3.3 Payoffs

At every terminal node, payoffs were allocated. Payoffs represent the total cost of each pathway from the decision node until that terminal node. The payoffs were calculated by adding the cost variables that were used within each pathway to determine the total cost per patient entering that pathway.

3.8 Data Analysis

3.8.1 Analysis of Ethnographic Observations

A distinguishing feature between qualitative and quantitative research is that in qualitative research, data analysis is a continuous process as it is performed both during and after data collection. Inductive Analysis was used to analyse the ethnographic observations that were conducted.

After each observation, the data collected was organised and divided into small sections based on different concepts and transcribed onto Excel so that it would be easy to analyse. Data coding then occurred, which involved first identifying segments in the data. Each segment represented one concept or an essential aspect of information and was then assigned to a minimum of one code that describes the segment. Once the codes were allocated to the segments, a list of all the codes used in each section was formulated and analysed to remove codes that were repeated and then sorted into the important codes, major codes and minor codes. Codes which were similar were grouped together into a category which was then named to describe the group of codes. The relationships between the categories were then studied in order to find patterns in the data. These patterns were then used as a basis for describing the results and informed the quantitative research that followed.

3.8.2 Analysis of Retrospective Records and Antibiotic Utilization Review

3.8.2.1 Retrospective Patient Data Analysis

The retrospective records of the patients that were identified to have MRSA in the two wards in 2013 were accessed from the Hospitals Medical Records Room. Once the data collected from the patients' retrospective records was entered onto Excel templates, they were sorted according to demographic, antibiotic and microbiology laboratory test data per ward.

3.8.2.1.1 Antibiotic Utilization Review

Within the patients' retrospective records, there were doctors' prescription charts and nurses' administration charts showing all the medication that was prescribed and administered to the patient. For each patient, the antibiotics on these charts were recorded on the patient's individual case report form, transferred to an Excel spread sheet and then summarised below. It was found that many of the prescriptions were incomplete and therefore assumptions had to be made and some antibiotics had to be excluded due to insufficient data. These assumptions are discussed in Section 5.9.

The total number of antibiotic prescriptions per ward was calculated and then analysed by sorting them into three different types: Empiric, MRSA-Specific and Other Antibiotics. The range, median, average and total number of each type of antibiotic administered per ward was calculated.

For each antibiotic administered the following analysis per ward was then conducted:

- The range, median and average number of days of administration
- The number of patients that received the antibiotic
- The number of prescriptions for the antibiotic

Lastly, for each antibiotic the Prescribed Daily Dose (PDD) of each antibiotic administered to each patient was calculated and compared to the WHO DDD. The DDD used in this study were last updated on 19 December 2013 (World Health Organization Collaborating Centre for Drug Statistics Methodology, 2013) .

3.8.2.1.2 Microbiology Laboratory Test Data Review

Within the patients' retrospective records, there were printouts of NHLS laboratory test results or tables in which the HCPs recorded the laboratory test results. However, the print-outs were not always present and the tables were not always complete. Therefore, to determine and analyse the NHLS laboratory tests that isolated MRSA in the study population, the data received from the NHLS Information System was used and not the NHLS laboratory tests in the patient records, although these were used to cross-reference in the case of missing data.

For each ward the following analysis was conducted regarding the microbiology laboratory tests that isolated MRSA:

- Total number of tests per ward
- Range and average number of tests per patient
- Percentage of the different types of specimens that isolated MRSA

3.8.3 Cost Analysis Cost Calculations

Various cost calculations were conducted using the costing databases in conjunction with the antibiotic utilization data obtained from the patients' retrospective records and the information received from the NHLS Information Systems regarding the NHLS laboratory tests that isolated MRSA in the study population. Costing calculations were conducted separately for each ward.

3.8.3.1 Antibiotic Cost Calculations

The daily cost and the total utilization cost was calculated for each antibiotic administered to each patient in each ward. The daily cost was the cost of the antibiotic per day per patient and was calculated by multiplying each patient's prescribed daily dose by the cost of that antibiotic. The total utilization cost was the total cost of the antibiotic administered to the patient and was calculated by multiplying the patient's daily cost by the number of days that the antibiotic was administered to the patient. The daily costs were then categorised as the daily cost of Empiric Antibiotics, the daily cost of MRSA-Specific Antibiotics and the daily cost of Other Antibiotics.

The average daily utilization costs and the average total utilization cost for each of the different antibiotics administered were also calculated per ward. For each different antibiotic, the average daily utilization cost was calculated by adding each patient's daily utilization cost for that antibiotic and dividing it by the number of patients that received that antibiotic. The average total utilization cost was calculated for each different antibiotic by adding each patient's total utilization cost and dividing it by the number of patients that received that antibiotic.

Thus the following antibiotic cost-utilization calculations were done for each patient in the study population:

- Daily utilization cost per patient:
  - per antibiotic (cost of antibiotic x patient's daily dose)
    - per Empiric Antibiotic
    - per MRSA-Specific Antibiotic
    - per Other Antibiotic
  - of all antibiotics administered (sum of Daily utilization cost per antibiotic per patient)
    - of all Empiric Antibiotics administered
    - of all MRSA-Specific Antibiotics administered
    - of all Other Antibiotics administered
- Total utilization cost per patient:
  - per antibiotic (cost of antibiotic x patient's daily dose x duration)

- all antibiotics administered (sum of Total utilization cost per antibiotic per patient)

For each ward in the study population the following antibiotic cost-utilization calculations were done:

- Total and average cost of:
  - the daily utilization cost (sum of each patient's daily utilization cost)
  - the Empiric Antibiotic daily utilization cost
  - the MRSA-Specific Antibiotic daily utilization cost
  - the Other Antibiotic daily utilization cost
  - the total utilization cost (sum of each patient's total utilization cost)

For each antibiotic used in the study population the following calculations were done for each ward:

- The average number of days for which that antibiotic was used
- The average cost per day of the antibiotic
- The average total cost of the antibiotic

3.8.3.2 NHLS Laboratory Test Cost Calculations

Using the information received from the NHLS Information System, the hospital numbers of the patients that isolated MRSA in the orthopaedic and vascular wards were selected. The laboratory test numbers that were allocated to each of these patient hospital numbers were identified. On the costing information sheet, the laboratory test number was used to identify all the steps and respective costs that were associated with that laboratory test. This was done for each laboratory test number. The calculated cost of each laboratory test was then allocated back to the patient hospital number that had that test. To maintain patient confidentiality and anonymity, the actual laboratory test numbers were changed to allocated laboratory test numbers (for example LT601, LT602) in this study.

This had to be done as the cost of each laboratory test differed due to a variation in the steps that were conducted in each laboratory test. The sum of all the laboratory tests conducted for each patient was then calculated. The costs were also separated into Microscopy cost and Culture and Sensitivity costs.

The following laboratory test cost-utilization calculations were done for each patient in the study population:

- Cost per NHLS laboratory test per patient (based on the laboratory test number)
- Cost of only microscopy per NHLS laboratory test per patient
- Cost of only culture and sensitivity per NHLS laboratory test per patient

- Total cost of all NHLS laboratory tests used per patient
- Total cost of only microscopy in all NHLS laboratory tests used per patient
- Total cost of only culture and sensitivity in all NHLS laboratory tests used per patient

For each ward in the study population the following laboratory test cost-utilization calculations were done:

- Average cost of one NHLS laboratory test
- Average cost of microscopy for one NHLS laboratory test
- Average cost of culture and sensitivity for one NHLS laboratory test
- Total and average cost of all NHLS laboratory tests used
- Total and average cost of only microscopy in all NHLS laboratory tests used
- Total and average cost of only culture and sensitivity in all NHLS laboratory tests used

3.8.3.3 Antibiotic Utilization plus NHLS Laboratory Tests Cost Calculations

For each patient the sum of the total cost of antibiotics administered and the total cost of NHLS laboratory tests conducted that isolated MRSA was calculated to obtain the total Antibiotic Utilization and NHLS Laboratory Test cost per patient.

3.8.4 Analysis of the Decision-Tree-Analytic Models

Once the structures of the decision-tree-analytic models were complete, the models were analysed by performing Rollback, Rankings, Tornado and Sensitivity Analysis. The analysis of each model was interpreted to assess the effects of the different variables, probabilities and pathways in the tree. The analysis of the models were then compared to evaluate the differences in costs in order to ultimately assess whether using the current Conventional Culture Method or the Xpert MRSA tests for MRSA would be cost-saving in the current setting. The preference set for the models was simple single-attribute calculations, with the optimal path for decisions being low.

3.8.4.1 Rollback and Rankings

The decision-tree-analytic models were first analysed by performing the Rollback analysis which calculated the expected values of each node. It is important to note that decision-tree calculations are performed backwards, from right to left. Thus it is termed rollback, as the values of each pathway are rolled back from the terminal node back to the decision node in order to present an expected value for each pathway. The payoff values and path probability were calculated at each terminal node and the expected values were calculated at each chance node. The expected value of the ideal pathway was shown at the decision node and the ideal pathway was also indicated as a coloured branch, with the non-ideal pathways represented by two slash marks (TreeAge Software INC, 2013).

By selecting the decision node and performing a Ranking Analysis, a text report was generated which ranked the various alternative pathways from the decision node along with their expected values. The rankings analysis also showed the incremental value which was the difference between two pathways. The strategy with the highest ranking was essentially the optimal pathway with the lowest cost.

The Ranking Analysis was performed for each model and then tabulated in order to compare the rankings of the different pathways depicted in the models.

3.8.4.2 Sensitivity Analysis

One-way Sensitivity Analyses were conducted for each variable in each of the decision-tree-analytic models. This process was conducted for all four decision-tree-analytic models. Once all the One-way sensitivity analyses were completed, the graphs were interpreted and discussed.

3.8.4.3 Tornado Analysis

The one-way sensitivity analyses of all the variables from a particular decision-tree-analytic-model could be represented in a single graph called a Tornado Diagram. Each variable in the decision-tree-analytic model was displayed in the Tornado Diagram as a different- coloured horizontal bar. The range of the expected values that were created when varying the variable was represented by the length of the bar, as the x-axis of the Tornado Diagram showed the expected value. Variables that were potentially the most uncertain and had a great effect on the expected value were represented as wide bars on the Tornado Diagram and were situated at the top of the diagram. The rest of the variables were also arranged and displayed in an order causing the narrowest bar to be situated at the bottom of the diagram closest to the x-axis.

4. RESULTS

4.1 Study Population

The study population consisted of all patients in an orthopaedic ward and vascular ward at CMJAH in 2013 that were identified as having isolated MRSA according to the data received from the NHLS data information systems.

4.1.1 Patient Characteristics and Demographic Data

The demographic data of the patients in the study population was obtained from their retrospective records. The data from the two wards was not directly compared as they are two different types of clinical wards and the patients presented with different clinical conditions.

4.1.1.1 Orthopaedic Ward

From the 18 patients that were identified to have MRSA in the orthopaedic ward in 2013, two of these patients' retrospective records were inaccessible from the Hospital's Medical Records Room. Thus, the demographic data and patient characteristics of the 16 patients relating to gender, age, length of stay in hospital, diagnosis and operations was summarised. The ages of the patients ranged from 17 years to 70 years, with an average age of 47 years and 68.75% were male. The length of stay in hospital per patient was calculated by counting the number of days between their date of admission and date of discharge. The average length of stay of a patient with MRSA in the orthopaedic ward was 48 days, but length of stay ranged from 17 days to 97 days as shown in Table 2. When looking at the main diagnosis of the patients, presented in Table 3, 62.50% had chronic osteomyelitis and 31.25% recorded a form of sepsis. For some of the patients more than one diagnosis and operation was recorded on their discharge sheet. Diagnoses and operations that occurred in one patient only were classified as Other. 56.25% of the patients had DRI (Debridement, Reaming and Irrigation) operations and 31.25% of the patients underwent an operation to remove a nail, plate or prosthesis.

Table 2: Age and Length of Stay in Hospital of the Patients in the Study Population in the Orthopaedic Ward in 2013

n=16	Range	Median	Average
Age (Years)	17 - 70	45	47
Length of Stay (Days)	17 - 97	41	48

Table 3: Number of Patients with Common Diagnoses, Operations and Procedures Performed in the Study Population in the Orthopaedic Ward in 2013

	Number of Patients
Diagnosis	
Chronic Osteomyelitis	10
Arthritis	2
Sepsis	5
Other	6
Operation / Procedure	
Remove Nail/plate/prosthesis	5
DRI	9
Debridement	4
Revision	2
Arthrotomy	2
Amputation	2
Other	6

4.1.1.2 Vascular Ward

Thirty-six patients in the vascular ward were identified as having MRSA in 2013. However, seven of these patients' retrospective patient records were excluded due to missing data. The demographic data and patient characteristics of the 29 patients relating to gender, age, length of stay in hospital, diagnosis and operations was summarised and shown in Table 4 and Table 5. The age of the patients ranged from 39 years to 89 years with an average age of 61 years and 75.86% of the patients were male. The length of stay in hospital per patient was calculated by counting the number of days between their date of admission and date of discharge. The average length of stay of a patient with MRSA in the vascular ward was 38 days, but the length of stay ranged from four days to 125 days for a patient who had multiple conditions including severe sepsis and nosocomial pneumonia before passing away. Diabetes mellitus and hypertension were commonly diagnosed in these patients and were thus excluded when summarising their diagnoses. Some patients had more than one diagnosis and operation recorded on their discharge sheet. Diagnoses and operations that were only present in one patient were classified as Other. 37.93% of the patients had a form of sepsis, 34.48% had Peripheral Vascular Disease (PVD) and 37.93% had other diagnoses. 72.41% had either a Below-Knee Amputation or an Above-Knee-Amputation, 58.62% had debridement and 41.38% had other operations.

Table 4: Age and Length of Stay in Hospital of the Patients in the Study Population in the Vascular Ward in 2013

n=29	Range	Median	Average
Age (Years)	39 - 89	59	61
Length of Stay (Days)	4 - 125	35	38

Table 5: Number of Patients with Common Diagnoses, Operations and Procedures Performed in the Study Population in the Vascular Ward in 2013

	Number of Patients
Diagnosis	
PVD	10
Sepsis	11
Infra/Fem-Pop Disease	6
Ischemia	5
Other	11
Operation / Procedure	
Amputation	21
Debridement	17
Bypass	6
Formalisation	3
Superficial Skin Graft	3
Other	12

4.2 Ethnographic Observations

4.2.1 Clinical Ward Observations

Clinical observations were conducted in the orthopaedic ward and the vascular ward. From the data that was observed and collected, the clinical practices in the two wards were similar and therefore both clinical observations are described as one. Figure 5 outlines the various aspects that were observed and documented during the observations in the orthopaedic and vascular wards.

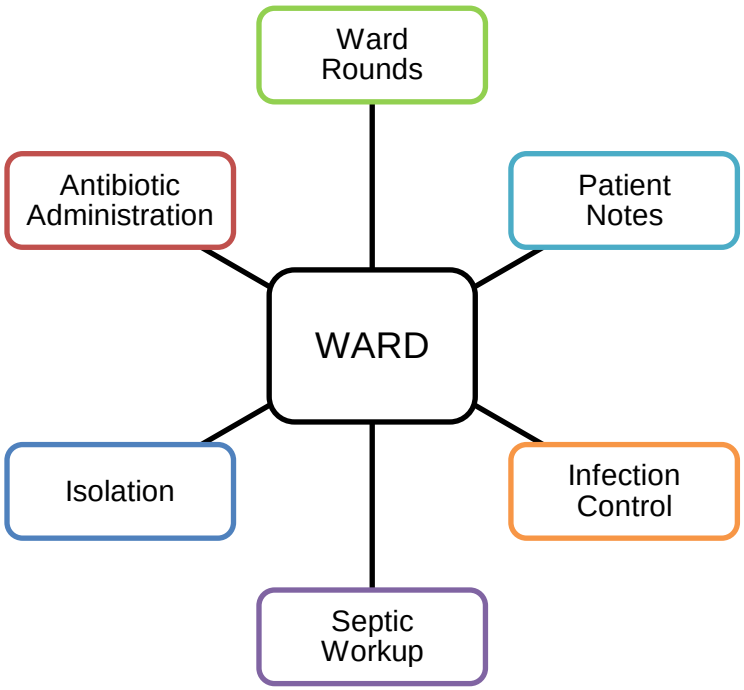


Figure 5: Various Clinical Aspects Observed in the Orthopaedic and Vascular Wards

4.2.1.1 Ward Rounds

A team of HCPs that conducted the morning ward rounds was observed. The team always consisted of the medical interns that were currently allocated to that ward and a nurse that was on duty in the ward. Doctors, specialists, consultants of the ward and other HCPs such as a radiologist and physiotherapist were also part of the team on some mornings.

4.2.1.2 Patient Notes

For each patient the medical intern greeted the patient and opened the patient's record to read the previous doctor's written notes. Some patients were asked about pain, current symptoms, or other brief questions related to the patient's condition. The intern also looked for any new laboratory test results, x-rays and current medication prescriptions in the patient's record and these were discussed with the team of HCPs on the current ward round. If a patient was recovering post-surgery, the patient's wound was checked or movement of the limb assessed. The medical intern then wrote the date and the key points from the ward round below the previous notes in the patient's record. The nurse present on the ward round wrote in her book the instructions discussed amongst the HCPs, for example, how often the patient's irrigation drip should be measured.

4.2.1.3 Infection Control

The use of antiseptic/disinfectant hand-rub and hand washing practices of HCPs during the wards was observed and documented. D-Germ hand-rub was placed on some of the

patient's bedside tables in the orthopaedic ward. In the vascular ward, a medical intern carried around a bottle of D-Germ hand-rub from patient to patient during the ward round. HCPs did not consistently use D-Germ hand-rub after consultation with each patient. In most cases, HCPs only used D-Germ hand-rub after physical contact with the patient and HCPs washed their hands after exposing and touching a patient's wound. It was common practice amongst the HCPs to use D-Germ at the end of the ward round.

On the walls of the wards there were posters regarding infection control Standard Precautions, with the following information:

- Applied to all patients at all times irrespective of diagnosis
- All body fluids (except sweat) are regarded as potentially infectious:
    - If it is wet, wear gloves
    - If it can splash/spray or aerolise wear a mask/goggles
    - Wear a gown or plastic apron
    - Wash hands:
        - Before and after patient care
        - After touching body fluids
        - After removing gloves
        - Before caring for another patient

During the routine morning ward rounds it was observed that PPE such as masks, gloves and gowns were infrequently used by HCPs. Gloves were worn if a wound was exposed or a drip was inserted or a specimen taken. The nurses wore disposable gowns and gloves when changing patients' bedding or wound dressings. There was no consistent protocol followed regarding the use of PPE in the wards.

4.2.1.4 Septic Workup

Routinely the nurse measured the patient's temperature twice daily. If the patient's temperature was above 37.5°C or the patient displayed symptoms of an infection, a septic workup was initiated. This included but was not limited to requesting a chest x-ray to determine the source of infection; taking a urine specimen and sending it to the microbiology laboratory for MCS; drawing blood for a full blood count; and testing for C Reactive Protein. The nurse usually administered a stat dose of paracetamol and depending on the severity of the patient's symptoms; a broad-spectrum Empiric Antibiotic was administered while waiting for the MCS laboratory test results. During ward rounds, the HCPs tried to follow up on the results of the MCS laboratory tests and often, if the results were not available, could not be found, or if the patient's symptoms deteriorated, the HCPs requested that another specimen

be taken and sent to the microbiology laboratory for MCS, which in some case resulted in unnecessary laboratory tests being conducted.

Once the patient's MCS laboratory results were available, their antibiotic prescription was changed accordingly by the HCPs, although this was subject to a time delay as the antibiotics would only be changed during the HCPs next ward round and certain antibiotics such as linezolid required that a consultant or senior doctor sign a motivation form before the antibiotic could be dispensed and administered to the patient.

4.2.1.5 Isolation

If a patient displayed signs of a serious infection and isolation of the patient was required, the patient was moved to a smaller room with only two beds in the ward. This room served as the patient's isolation. However, if a second patient also required isolation due to the same or different infection, and there were no other available small rooms, the second patient was placed in the same room as the first patient. If there were no smaller rooms available, the patient was placed in the corner of the main room in the ward.

4.2.1.6 Antibiotic Administration

Blood cultures were not done pre-operatively, but tissue specimens from operations and procedures were sent to the microbiology laboratory and the results sent back to the ward. In the orthopaedic ward, it was a common practice that post-operative patients received IV gentamicin until laboratory results reporting no infection were obtained. If the laboratory results reported an infection, the antibiotics were changed accordingly. Following the instructions from the HCPs during the ward rounds, the nurses also extracted fluid from the patient's wound irrigation system and sent it to the microbiology laboratory to check for infection.

In some cases there was a time delay, ranging from a few hours to a few days, between when the laboratory results were received indicating that a patient had MRSA and when the patient's antibiotics were changed to MRSA-Specific Antibiotics. In other cases, some patients did not receive MRSA-Specific Antibiotics.

The observations aided in gaining a clearer understanding of the daily clinical practices of HCPs regarding the current management of patients suspected of having an MRSA infection and the clinical pathways that follow, depending on whether the patient had MRSA or not. The knowledge gained from the observations greatly assisted in understanding and interpreting the patient records when looking at the retrospective patient records.

4.2.2 NHLS Microbiology Laboratory Observations

Observation at the Bacteriology Bench of the NHLS Microbiology Laboratory at CMJAH provided an explanation of the current method used when a sample for a suspected infection was received. The laboratory procedure, from when a specimen for a suspected infection was received until a confirmed diagnosis was made, was documented with special attention to the steps involved when a Gram-positive, *Staphylococcus aureus* or MRSA infection was suspected and detected.

4.2.2.1 Conventional Culture Process

The observations demonstrated that when a sample for a suspected infection was received in the laboratory, the Conventional Culture Method was used to determine the type of infection. The Conventional Culture Method has three main steps: Microscopy, Culture and Sensitivity, commonly referred to as “MCS”. However, to clearly describe the observations, two additional preparation steps were included. Therefore, all five steps are listed in Figure 6 and thereafter each step is explained.

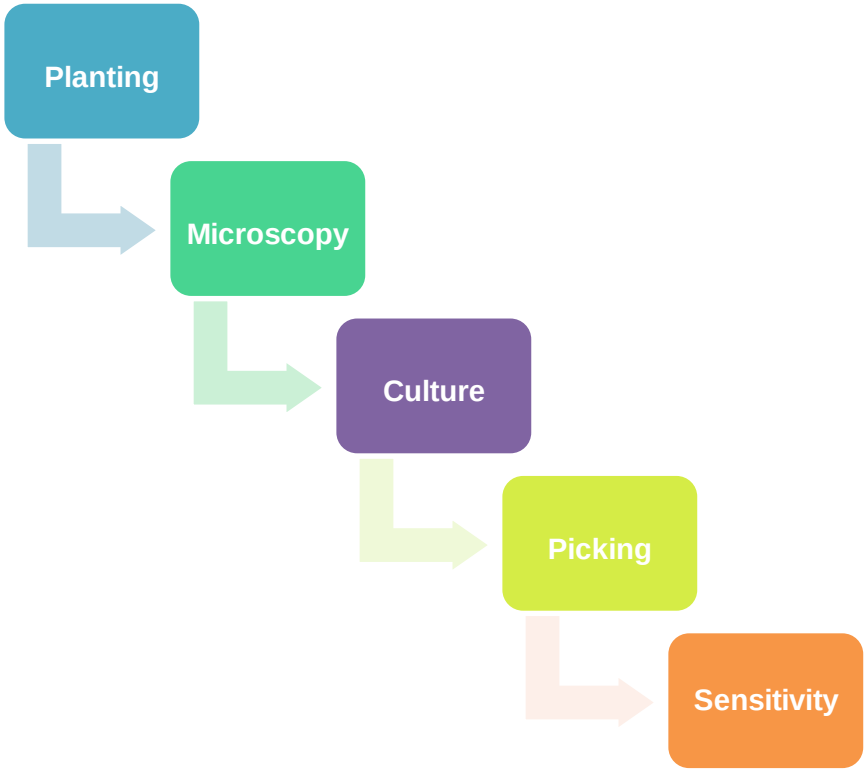


Figure 6: Steps Involved in the Conventional Culture Method

4.2.2.1.1 Planting

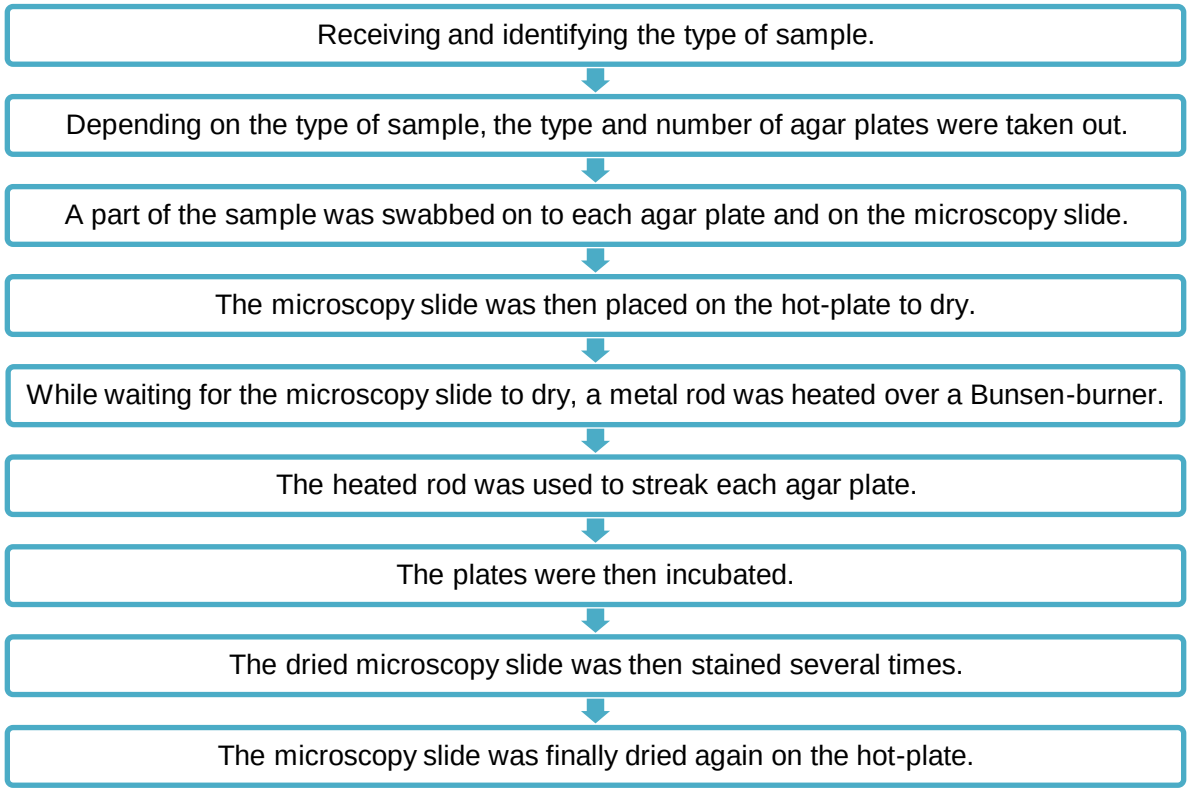


Figure 7: Process Involved in the Planting Step

The first step of the Conventional Culture Method in the microbiology laboratory was referred to as “Planting” and is explained in Figure 7. The process of staining the microscopy slide was: firstly, crystal violet was applied for one minute and then rinsed with water; secondly, Gram's iodine was applied for one minute and rinsed with water; thirdly, Gram's decolourize was applied for ten seconds and rinsed with water; lastly, Gram's safranin was applied for 30 seconds and rinsed with water. The complete process of Planting took approximately ten minutes per sample.

4.2.2.1.2 Microscopy

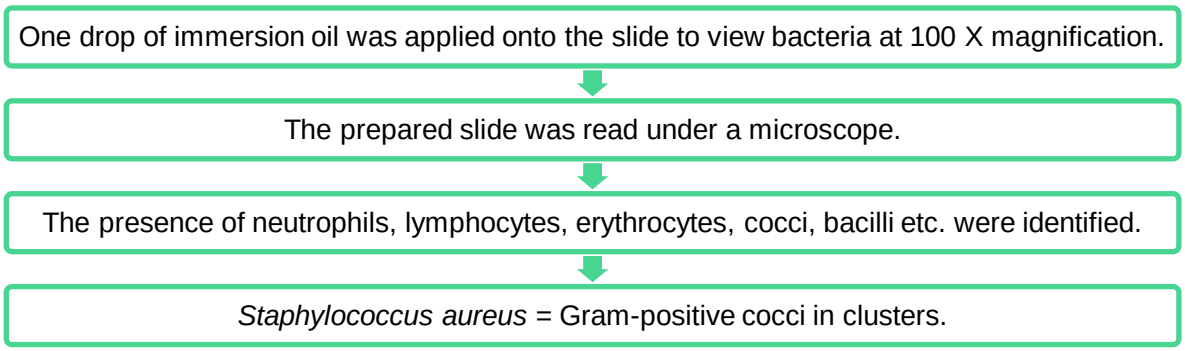


Figure 8: Process Involved in the Microscopy Step

The second step observed was “Microscopy” which is outlined in Figure 8. The identified were cells and bacteria were recorded on the working card for each sample. *Staphylococcus*

aureus presents as Gram-positive cocci in clusters under the microscope. The process of microscopy took approximately five minutes.

4.2.2.1.3 Culture

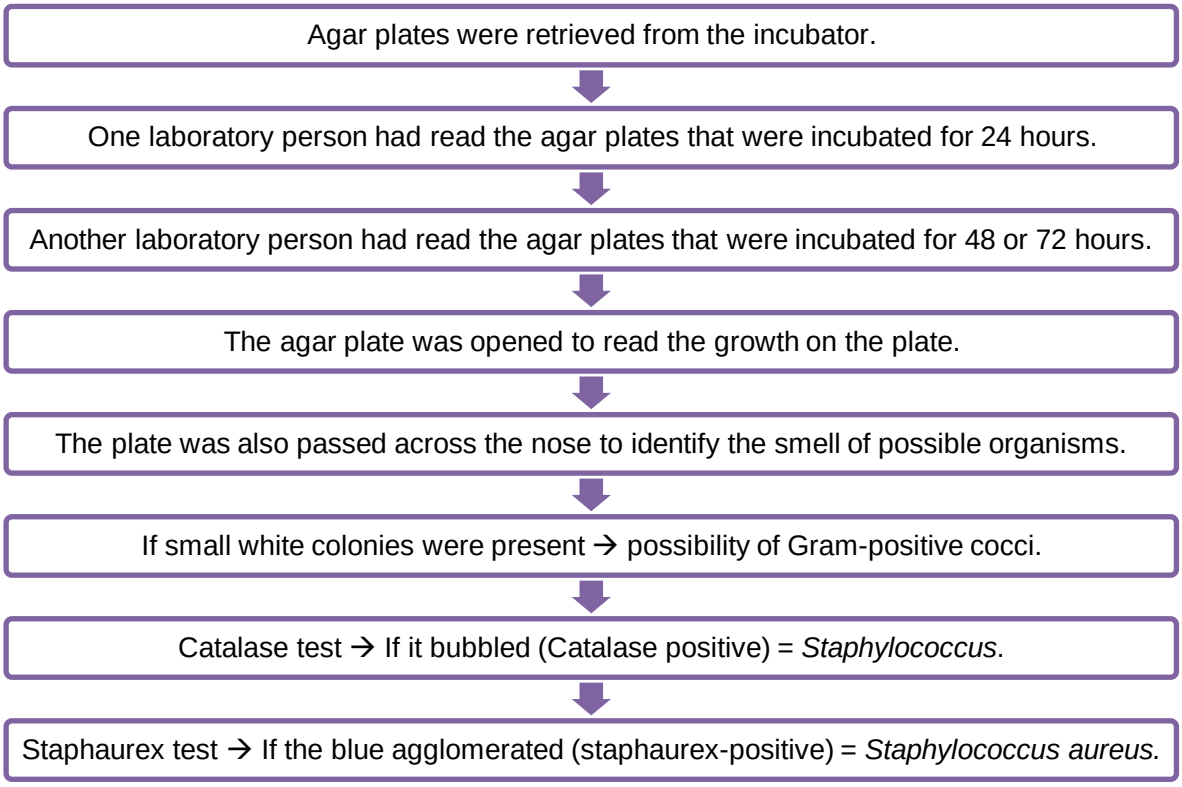


Figure 9: Process Involved in the Culture Step

The third step observed was “Culture” and is unfolded in Figure 9. The following was observed for one plate focusing on the identification of *Staphylococcus aureus*. If small white colonies were present, there was a possibility of Gram-positive cocci, which required a catalase test to be conducted to identify if it was a *staphylococcus* or *streptococcus* infection. Working on the MacConkey agar plate, a pin was used to pick from the agar and the picked agar was placed on the lid of the plate. One drop of catalase reagent (hydrogen peroxide) was placed on the picked agar on the lid. If it bubbled, it was termed catalase-positive, which indicated that it was *staphylococcus*. If it did not bubble, it was termed catalase negative, which indicated that it was *streptococcus*. If it was catalase-positive, the staphaurex test was then performed. One drop of staph xtra latex was placed on the test card. The mixing stick was used to pick from the agar and then rubbed on the test card. If the blue agglomerated, it was termed staphaurex-positive, which indicated that it was *Staphylococcus aureus*. If there was no growth of fine growth on the agar plates, the plates were incubated for a further 24 hours. If there was mixed growth, sub-culturing was performed. The results were entered on the corresponding working card. The culture step took place over approximately five to ten minutes per plate.

4.2.2.1.4 Picking

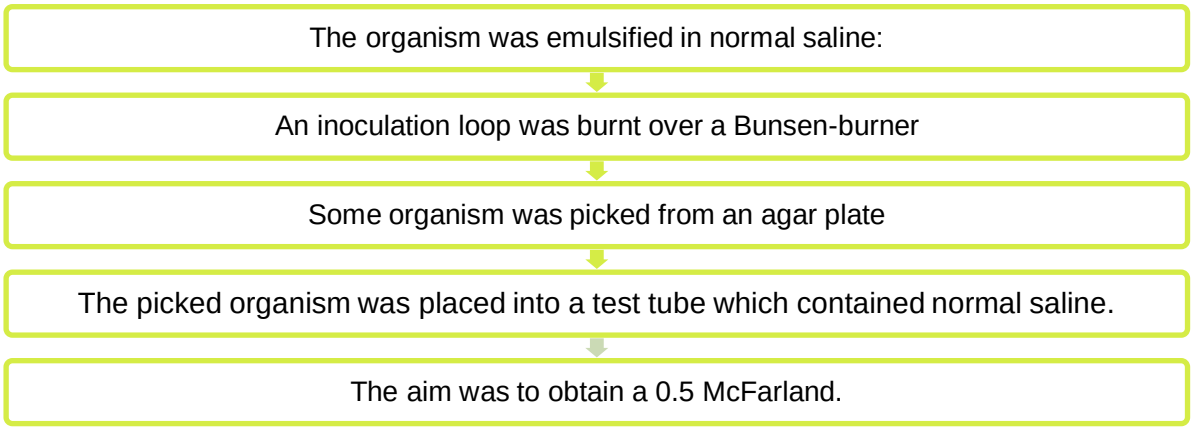


Figure 10: Process Involved in the Picking Step

If *Staphylococcus aureus* was identified, the next step observed was "Picking" as described in Figure 10. A heavy inoculum (adding too much organism) was avoided as it could lead to a false MRSA reading. Picking took approximately two minutes.

4.2.2.1.5 Antibiotic Sensitivity

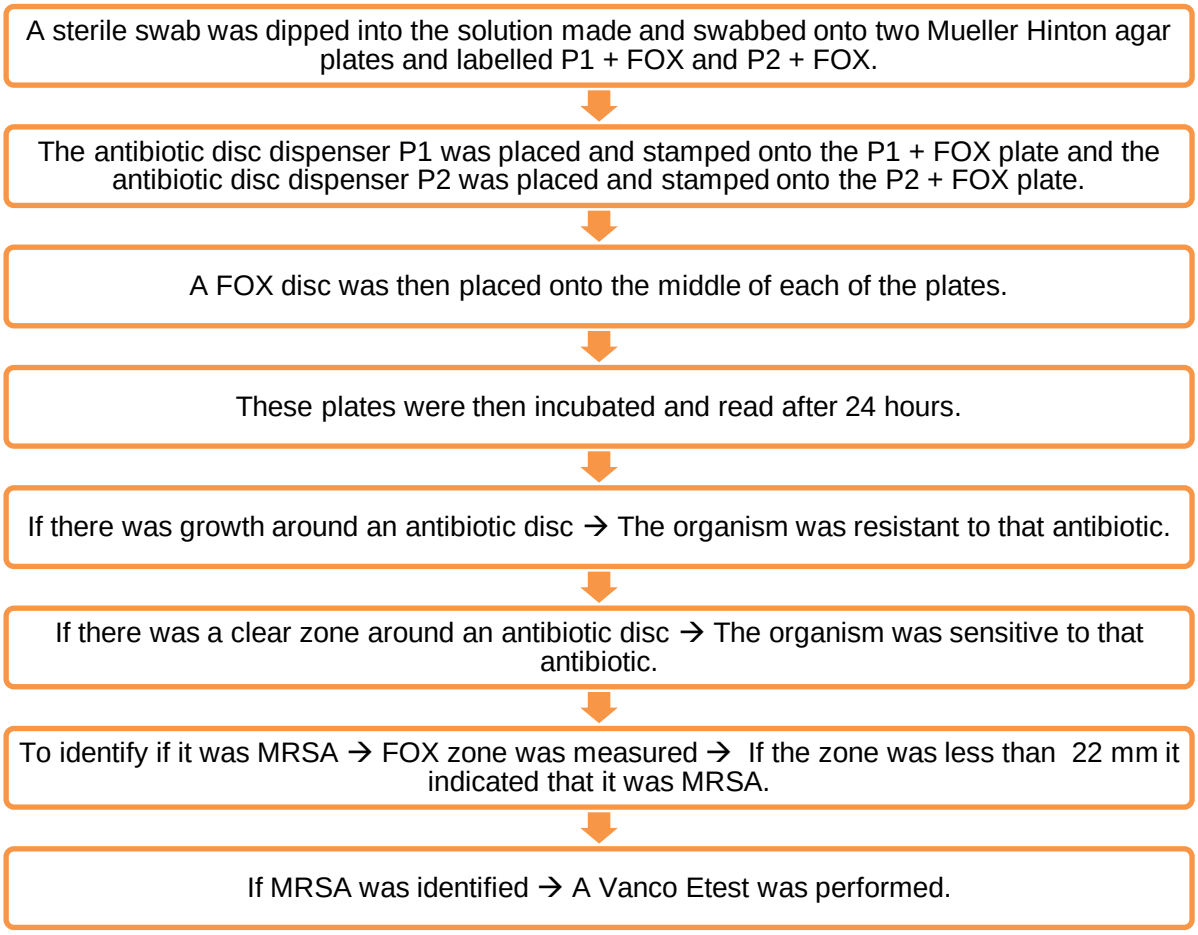


Figure 11: Process Involved in the Antibiotic Sensitivity Step

The final step of the Conventional Culture Method was “Antibiotic Sensitivity” using the disc diffusion method as shown in Figure 11. The preparation of the antibiotic sensitivity plates for incubation took about five minutes. After incubation, to identify if it was MRSA, the FOX (Cefoxitine) zone was measured. If the zone was greater than 22 mm it indicated that it was *Staphylococcus aureus*. If the zone was less than 22 mm it indicated that it was MRSA. The results were then entered onto the corresponding working card; this process took approximately two minutes.

If MRSA was identified, the zone size of the vancomycin disk was not measured. Rather, a Vanco Etest was performed. This was done by blood agar being picked from a plate that had the organism; an inoculum of 0.5 McFarland in normal saline was prepared; the solution was swabbed on an agar plate; the Etest strip was placed on the plate and then the plate was incubated. After 24 hours the plate was read, the results were entered on the corresponding working card; this process took approximately two minutes.

Once the laboratory personnel had worked with the required samples and plates in each step, they transferred the daily results from the working cards onto a computer system which was accessible to the doctors as provisional results. Once all tests and readings had been performed for a sample, after 48 to 72 hours depending on the type of growth, the results were checked by the pathologist and the results were finalised.

4.2.2.2 Timing Involved in the Conventional Culture Method

Before and after each step, the laboratory personnel swabbed the working bench with alcohol and wore gloves and a laboratory coat at all times. The laboratory personnel did not perform the complete process of MCS for each individual plate; rather they performed each step for all the plates before moving onto the next step. It was difficult to allocate an exact time to each step as the reading and interpreting of some plates took longer than others due to the growth patterns.

Table 6: Hands-on Time and Incubation Time Involved in the Conventional Culture Method at the NHLS Microbiology Laboratory at CMJAH

	Planting	Microscopy	Culture	Picking	Sensitivity
Hands-on Time (Minutes)	10	5	5 - 10	2	10
Incubation Time (Hours)	24		24		24

Therefore, as illustrated in Table 6, the hands-on time allocated to each time was not the exact time but rather the approximate and average time that the laboratory personnel spent performing that process for one specimen. The incubation time was also not always standard as additional incubation time was required depending on the growth of the organisms, or further process that needed to be performed. The culture process was performed after initial incubation of 24 hours and thereafter performed again once the plates were incubated for 48 hours and 72 hours if required. For the Antibiotic Sensitivity process an additional 24 hour incubation period was added if a Vanco Etest was performed.

The observations at the bacteriology bench of the NHLS Microbiology Laboratory at CMJAH assisted in understanding and interpreting the patient records when looking at the retrospective patient records. The observations also helped gain an understanding of why a definite time cannot be allocated to the process, as well as an awareness of the numerous amounts of resources involved in this process. Thus, these observations informed the type of enquires and research to be conducted using the qualitative research methods that follow in the rest of the study.

4.2.3 Antibiotic Dispensary Observations

Information regarding the current antibiotic dispensing policies for inpatients was obtained by observations and assistance from the pharmacist in charge of the antibiotics designated area at CMJAH's main dispensary. The main dispensary at CMJAH has a designated room for the storage and dispensing of antibiotics. Access is restricted unless a pharmacist is present and there is a designated Antibiotics Stewardship pharmacist in charge.

There were no written protocols available regarding the general policies used for dispensing antibiotics to inpatients at CMJAH. The pharmacist said that they mainly follow the decisions of the Pharmacy and Therapeutic Committee and this may differ between wards within CMJAH and between hospitals.

4.2.3.1 Prescribing and Dispensing of Antibiotics

The process of prescribing and dispensing antibiotics to inpatients was explained by a pharmacist. In the wards, the doctors prescribe antibiotics on the patient's prescription chart. The nurse then copies the prescription onto a dispensary order form and attaches the relevant signed motivation forms. If the antibiotic for a patient was urgent, the nurse would bring the order form to the dispensary and take the medication back to the ward. If the antibiotic for a patient was not urgent, runners fetched the forms from the wards and later delivered the antibiotics to the wards. Depending on the availability of stock of the requested antibiotics, the dispensary normally dispensed three, five or seven days' supply of the

antibiotic prescribed for the patient. It was then the duty of the nurse to manage the antibiotics in the ward. On Tuesdays and Wednesdays the dispensary dispensed antibiotics for seven days. On Mondays, Thursdays and Fridays the dispensary dispensed antibiotics for five days. If a new patient was admitted and needed antibiotics during the weekend, the antibiotics were administered if there were extra antibiotics available in the ward, or they were taken from the emergency cupboard or, if there were none, a pharmacist would be called in. If there were remaining antibiotics from one patient, they were often used for another patient requiring the same antibiotic but waiting for theirs to arrive. However, antibiotics were mainly dispensed on a per-patient basis. A small quantity of antibiotics such as metronidazole, cloxacillin and clindamycin were kept as ward stock. The dispensary did not receive many prescriptions for antibiotics from the orthopaedic ward, as the orthopaedic ward ordered most of their Empiric Antibiotics in bulk once a week.

4.2.3.2 Restricted Use

Due to the potential for misuse of antibiotics, certain antibiotics had restricted use and the dispensary required stipulated documents before dispensing them. Table 7 provides an example of the restricted dispensing of antibiotics at CMJAH based on the information obtained from the pharmacist.

Table 7: Example of Restricted Dispensing of Certain Antibiotics at CMJAH

Antibiotic	Motivation Required	Authorisation	Laboratory Results Required
Vancomycin	Yes	Prescribing Doctor and Consultant	No
Linezolid	Yes	Certain Consultants only	Yes
Carbapenems	Yes	Prescribing Doctor and Consultant	Yes

For vancomycin, the dispensary required a motivation form to authorise the prescription. The form had to have two signatures, one from the prescribing doctor and one from the consultant. If the consultant was unavailable, any senior doctor could sign and authorise the form. Laboratory results were not required for vancomycin to be dispensed. In contrast, the dispensary was strict with dispensing linezolid. Microbiology laboratory results were first required and linezolid was dispensed only if there were no Other Antibiotics that could be used, as it was more expensive compared to vancomycin. With regard to meropenem, imipenem and ertapenem, microbiology laboratory results were also required before these antibiotics were dispensed. However, the dispensary was flexible and it depended on each individual patient's case.

4.2.3.3 Antibiotic Stewardship

Observations as well as enquiry in the wards and dispensary revealed the following about the existing Antibiotic Stewardship programme at CMJAH:

- The pharmacists were not actively involved in the programme.
- The pharmacist felt that if they were actively involved and present during the ward rounds they would be able to improve the current Antibiotic Stewardship programme. They would be able to guide prescribing and immediately inform the doctors if certain antibiotics were out of stock and to prescribe an alternative to prevent a delay in treatment.
- When a pharmacist does not dispense certain antibiotics or has certain requirements before dispensing, at times the doctors and nurses would disagree with the pharmacist and feel that the pharmacist was denying the use of antibiotics or did not trust the doctor's judgment. However, if a pharmacist was actively present in the ward they would be able to explain their reasoning.
- A pharmacist would also be able to oversee the manner in which the antibiotics were controlled and administered in the ward as the ward often returns expired antibiotics which is wasteful as the antibiotics could have been used for patients in other wards.
- If pharmacists do become involved in the wards, it was felt that more pharmacists would be needed and clinical pharmacologists would need to be introduced.

4.2.4 Qualitative Analysis of Ethnographic Observation

Inductive analysis was used to analyse the information obtained from the observations Table 8, Table 9 and Table 10 are the summarised tables of the codes and categories along with explanations and the patterns derived from the observations in the wards, NHLS Microbiology Laboratory and Antibiotic Dispensary. The detail tables that were used to list all the codes to classify them in their respective categories are shown in Appendix 6 (Table 34, Table 35 and Table 36).

4.2.4.1 Clinical Ward Observations

Table 8: Summarised Codes and Categories Identified from the Ethnographic Observations in the Clinical Wards at CMJAH

Categories	Codes
Communication	HCP-HCP; HCP-Patient; HCPs; Ward Rounds; Nurses
Routine	Ward Rounds; Nurses
Patient Records	Ward Rounds; Doctors' Notes; Prescriptions; X-rays; NHLS reports
Infection	HCP-Patient; Ward Rounds; Nurses; Antiseptic hand rub; Hand-

Control	washing; PPE; Isolation
Antibiotics	NHLS Report; Empiric; Changed; Authorisation; Pre/Post-op
Inconsistent	HCPs; Doctors Notes; Anti-septic hand rub; Hand-washing; PPE; Protocols
Specimens for MCS	NHLS Reports; Redone; Pre/Post-op; Wound Irrigation; Confirmed; Suspected
Delay	Prescriptions; NHLS Reports; Empiric; Change; Authorisation; Isolation
Infection	NHLS Reports; Empiric; Pre/Post-op; Suspected; Confirmed; Isolation

Based on the codes and categories in Table 8, patterns regarding the observations at the wards were deduced. The main patterns identified were Underlying Themes and Daily Practices. The Pattern of Daily Practices included the observed daily practices of HCPs regarding Infection Control, Specimens for MCS, Antibiotics and Patient Records. The pattern of Underlying Themes consisted of Routine, Communication, Inconsistent, Delay and Unavailable.

4.2.4.2 NHLS Microbiology Laboratory Observations

Table 9: Summarised Codes and Categories Identified from the Ethnographic Observations in NHLS Microbiology Laboratory at CMJAH

Categories	Codes
Suspected MRSA Infection	Specimen; Gram-positive cocci in clusters; Catalase-positive; *Staphylococcus*; Staphaurex-positive; *Staphylococcus aureus;* FOX Zone; Vanco Etest
Conventional Culture Method	Planting; Microscopy; Culture; Picking; Sensitivity; Vanco Etest
Hands-on Time	Ten minutes; Five minutes; Five to ten minutes; Two minutes; Ten minutes
Incubation Times	24 Hours/48 Hours/72 Hours; 24 Hours; 24 Hours
Results	Recorded; Working card; Computer system; Provisional; Checked; Finalised
Disposable Resources	Agar plates; Swab; Microscopy slide; Stains; Water; Immersion oil; Catalase test kit; Staphaurex test kit; Saline; Antibiotic discs; Etest strip
Fixed Resources	Microscope; Hot-plate; Metal rods; Inoculation loops; Test tubes; Bunsen-burner; Incubator; Antibiotic disc dispensers

From the codes and categories in Table 9, two important patterns relating to the observations at the NHLS Microbiology Laboratory were identified. The first pattern was time, which included hands-on time, which was the time spent by the laboratory personnel physically performing the processes and the incubation time which was the time that the agar plates had to be kept in the incubator. This pattern highlighted that not only is the Conventional Culture Method a lengthy process, it is a laborious process as well. The second pattern was the resources involved in performing the Conventional Culture Method, which was categorised as Disposable resources, those that were needed per specimen tested and fixed, or Capital resources. This pattern emphasised the amount of resources required to perform one test.

4.2.4.3 Antibiotic Dispensary Observations

Table 10: Summarised Codes and Categories Identified from the Ethnographic Observations in Antibiotic Dispensary at CMJAH

Categories	Codes
Protocols	Not written; Differ; Per-patient; Ward; Dispensary
Prescribing	Per-patient; Ward; Doctors; Patient's prescription chart; Dispensary order form; Motivation
Dispensing	Per-patient; Ward; Motivation; Runners; Dispensary; Waiting; Three/five/seven days
Nurses	Dispensary order form; Manage ward stock; Administer; Emergency cupboard; Roll-over
Urgent	Emergency cupboard; On-call; Roll-over
Authorisation	Per-patient; Doctors; Motivation; Restricted; Waiting; Vancomycin; Linezolid; Carbapenems; MCS results
Antibiotic Stewardship	Ward; Doctors; Dispensary; Pharmacist inactive; Advantages; Out of stock; Expired; Communication
Problems	Waiting; Out of stock; Expired; Communication

Patterns of Current Procedure and Improvement were derived from the codes and categories in Table 10, from the observations at the antibiotics designated area of the main dispensary. The patterns were a basic emphasis of the Current Procedures involved in Prescribing, Dispensing and Authorisation as compared to the need for Improvement in the areas of Antibiotic Stewardship, Protocols and the current Problems Identified. The patterns revealed the manner in which the observed practices were carried out and suggested areas that needed further investigation using qualitative research methods.

4.3 Retrospective Records and Antibiotic Utilization Review

4.3.1 Antibiotic Utilization Review

4.3.1.1 Orthopaedic Ward

A total of 103 antibiotic prescriptions were recorded for the 16 patients that had MRSA in the orthopaedic ward in 2013. However, 23 (24.27%) of these antibiotic prescriptions were excluded due to missing information. Therefore, a total of 78 antibiotic prescriptions were administered to the 16 patients. These 78 prescriptions were analysed and summarised in Table 11.

Table 11: Number of Antibiotics Administered per Patient and in Total in the Orthopaedic Ward in 2013

Number of Antibiotics Administered	Per Patient			Orthopaedic Ward
	Range	Median	Average	Total
Empiric Antibiotics	1 - 7	2.50	2.75	44.00
MRSA-Specific Antibiotics	0 - 5	2.00	1.69	27.00
Other Antibiotics	0 - 2	0.00	0.44	7.00
All Antibiotics	2 - 9	4.00	4.88	**78.00**

Each patient was administered a range of two to nine antibiotics, an average of five antibiotics per patient. The antibiotics administered were divided into Empiric Antibiotics, MRSA-Specific Antibiotics and Other Antibiotics. Of the antibiotics administered, 56.41% were Empiric Antibiotics which consisted of co-amoxiclav, gentamicin, cloxacillin and cefazolin. A range of one to seven Empiric Antibiotics were administered to each patient with an average of three Empiric Antibiotics per patient. The only MRSA-Specific Antibiotics administered in this ward were vancomycin, linezolid and rifampicin, which made up only 34.62% of the total number of antibiotics. A patient received a range of between zero to five and an average of two MRSA-Specific Antibiotics. The remaining 8.97% were Other Antibiotics that were administered including cefotaxime, ertapenem, ciprofloxacin, ceftazidime and metronidazole.

From the 78 antibiotics that were prescribed and administered to the 16 MRSA-positive patients, there were 18 antibiotics that were administered at different strengths and routes of administration, of which 12 were different antibiotics. Cefazolin IVI was commonly used in the orthopaedic ward, as 62.50% of the patients received cefazolin IVI; 20.51% of the prescriptions were for cefazolin either intra-operatively or post-operatively. Gentamicin was commonly administered as an irrigation system in the orthopaedic ward (to 68.75% of patients). Although all 16 patients had MRSA diagnosed, only nine of these patients received

MRSA-Specific Antibiotics during their time in the ward. It was also common that rifampicin was administered to eight out of the nine patients that received vancomycin.

The number of days that an antibiotic was administered varied between the different antibiotics and patients, as shown in Table 12. Some patients received more than one prescription of the same antibiotics at different times during their time in hospital and this is also demonstrated in Table 12.

Table 12: Number of Days of Administration, Number of Patients and Number of Prescriptions per Antibiotic in the Orthopaedic Ward in 2013

Antibiotic	Number of Days		Number of Patients	Number of Prescriptions
	Range	Average		
Cefazolin IVI	1 - 12	2	10	16
Gentamicin Irrigation System	3 - 32	14	11	11
Vancomycin IVI	1 - 19	9	9	11
Rifampicin	4 - 19	12	8	8
Vancomycin Irrigation System	2 - 8	4	6	6
Cloxacillin Capsules	10 - 20	15	4	5
Cloxacillin IVI	1 - 10	5	3	4
Co-amoxiclav 625 mg Tablets	14 - 29	21	3	3
Co-amoxiclav 1 g Tablets	1 - 13	7	2	2
Co-amoxiclav 1.2 g IVI	4 - 6	5	1	2
Linezolid	1 - 6	4	2	2
Ertapenem IVI	1 - 6	4	2	2
Co-amoxiclav 0.6 g IVI	3	3	1	1
Cefotaxime	9	9	1	1
Metronidazole	7	7	1	1
Ciprofloxacin	32	32	1	1
Ceftazidime IVI	19	19	1	1
Ceftazidime Irrigation System	1	1	1	1

The doses of the antibiotics prescribed and administered to patients in the orthopaedic ward varied. Therefore, for each antibiotic prescribed and administered, the PDD was calculated and compared to the WHO DDD and is presented in Table 13. PDDs were not calculated for 18 antibiotic prescriptions that were administered via an irrigation system, as the corresponding WHO DDD for irrigation systems were not available. Out of the 60

prescriptions, 40% of the PDD were equal to the DDD and 40% of the PDD were higher than the DDD. The remaining 20% of the DDD were lower than the PDD.

Table 13: World Health Organization Defined Daily Dose (DDD) versus Prescribed Daily Dose (PDD) for Antibiotics in the Orthopaedic Ward in 2013

Antibiotic	WHO	Per Prescription	
	DDD (g)	PDD (g)	Number of Prescriptions
Vancomycin IVI	2.00	2.00	8
		1.00	2
		9.00	1
Linezolid oral	1.20	1.20	2
Amoxicillin 500 mg oral	1.00	1.75	2
		1.50	3
Amoxicillin 1 g IVI	3.00	1.50	1
		3.00	2
Rifampicin oral	0.60	1.20	7
		0.60	1
Cloxacillin oral	2.00	4.00	5
Cloxacillin IVI	2.00	2.00	1
		3.00	1
		4.00	2
Cefazolin IVI	3.00	2.00	4
		6.00	2
		1.00	4
		3.00	6
Ertapenem IVI	1.00	1.00	1
		1.00	1
Cefotaxime IVI	4.00	9.00	1
Metronidazole	1.50	1.20	1
Ciprofloxacin oral	1.00	1.00	1
Ceftazidime IVI	4.00	4.00	1

4.3.1.2 Vascular Ward

A total of 151 antibiotic prescriptions were recorded for the 29 patients that had MRSA in the vascular ward in 2013. However, 42 (27.81%) of these antibiotic prescriptions were excluded due to missing information. Therefore, a total of 109 antibiotic prescriptions were

administered to the 29 patients. These 109 prescriptions were then analysed and summarised in Table 14.

Table 14: Number of Antibiotics Administered per Patient and in Total in the Vascular Ward in 2013

Number of Antibiotics Administered	Per Patient			Vascular Ward
	Range	Median	Average	Total
Empiric Antibiotics	0 - 8	1.00	1.62	47.00
MRSA-Specific Antibiotics	0 - 4	0.00	0.72	21.00
Other Antibiotics	0 - 5	1.00	1.41	41.00
All Antibiotics	1 - 13	3.00	3.76	**109.00**

Each patient was administered a range of one to thirteen antibiotics with an average of four antibiotics per patient. The antibiotics administered were categorised into Empiric Antibiotics, MRSA-Specific Antibiotics and Other Antibiotics. Of the antibiotics administered, 43.12% were Empiric Antibiotics which consisted of piperacillin/tazobactam, co-amoxiclav, cloxacillin, gentamicin, amoxycillin and cefazolin. A range of zero to eight Empiric Antibiotics was administered to each patient with an average of two Empiric Antibiotics per patient. The only MRSA-Specific Antibiotics administered in this ward were vancomycin and rifampicin, which made up only 19.27% of the total number of antibiotics. A patient received a range of between zero to four and an average of one MRSA-Specific Antibiotics. The remaining 37.61% were Other Antibiotics that were administered including ertapenem, meropenem, imipenem, clindamycin, ciprofloxacin, metronidazole, ceftazidime, cefepime, clarithromycin, ciprofloxacin, cefuroxime, amikacin and co-trimoxazole.

From the 109 antibiotics that were prescribed and administered to the 29 MRSA-positive patients, there were 27 antibiotics that were administered at different strengths and routes of administration, of which 20 were different antibiotics. Piperacillin/Tazobactam was a commonly used Empiric Antibiotic in the vascular ward (37.93% of patients). Co-amoxiclav was also commonly administered to the patients in the vascular ward. Although all 29 patients were diagnosed with MRSA, only 11 of these patients received MRSA-Specific Antibiotics, of which all 11 patients received vancomycin and one patient received vancomycin and rifampicin during their time in the ward.

The number of days that an antibiotic was administered varied between the different antibiotics and patients and is shown in Table 15. Some patients received more than one prescription of the same antibiotics at different times during their time in hospital and this is also demonstrated in Table 15.

Table 15: Number of Days of Administration, Number of Patients and Number of Prescriptions per Antibiotic in the Vascular Ward in 2013

Antibiotic	Number of Days		Number of Patients	Number of Prescriptions
	Range	Average		
Vancomycin IVI 1 g	1 - 11	3	11	20
Piperacillin/Tazobactam	1 - 14	6	11	19
Co-amoxiclav IVI 1.2 g	1 - 20	6	13	14
Meropenem IVI 1 g	1 - 11	6	5	6
Cefepime IVI 1 g	2 - 9	5	5	5
Ertapenem IVI 1 g	1 - 4	3	4	4
Metronidazole IVI	5 - 11	7	4	4
Co-amoxiclav 625 mg Tablets	10 - 13	12	3	3
Meropenem IVI 500 mg	5 - 6	6	3	3
Imipenem IVI 1 g	1 - 5	3	1	3
Ciprofloxacin IVI	4 - 12	7	3	3
Gentamicin IVI	3 - 7	4	2	3
Co-amoxiclav 1 g Tablets	4 - 19	12	2	2
Cloxacillin IVI 1 g	4 - 13	9	2	2
Ceftazidime IVI 1 g	6 - 9	8	2	2
Metronidazole Tablets	2 - 4	3	2	2
Amoxycillin Capsules	1 - 13	7	1	2
Clarithromycin Tablets	1 - 6	4	1	2
Co-Trimoxazole	1 - 7	4	1	2
Clindamycin IVI 600 mg	17	17	1	1
Cloxacillin Capsules	3	3	1	1
Ciprofloxacin Tablets	9	9	1	1
Cefepime IVI 2 g	5	5	1	1
Rifampicin IVI	3	3	1	1
Amikacin	1	1	1	1
Cefuroxime IVI	3	3	1	1
Cefazolin IVI	1	1	1	1

For each antibiotic prescribed and administered in the vascular ward, the PDD was also calculated and compared to the DDD and is presented in Table 16. From the 109 prescriptions, 39% of the PDD were equal to the DDD and 39% of the PDD were higher than the DDD. The remaining 22% of the DDD were lower than the PDD.

Table 16: World Health Organization Defined Daily Dose (DDD) versus Prescribed Daily Dose (PDD) for Antibiotics in the Vascular Ward in 2013

Name	WHO	Per Prescription	
	DDD (g)	PDD (g)	Number of Prescriptions
Vancomycin IVI 1 g	2.00	0.50	2
		1.00	1
		1.00	6
		2.00	8
		3.00	1
		2.00	1
		4.00	1
Piperacillin 4 g	14.00	16.00	15
		12.00	1
		4.00	1
		8.00	2
Amoxicillin 1 g IVI	3.00	3.00	13
		4.00	1
Meropenem IVI 1 g	2.00	3.00	4
		2.00	1
		1.00	1
Cefepime IVI 1 g	2.00	3.00	1
		2.00	4
Ertapenem IVI 1 g	1.00	1.00	3
		2.00	1
Metronidazole IVI	1.50	1.50	4
Amoxicillin 500 mg oral	1.00	1.50	3
Meropenem IVI 500 mg	2.00	1.50	3
Imipenem IVI 1 g	2.00	2.00	1
		3.00	2
Ciprofloxacin IVI	0.50	1.20	1
		0.80	1
		4.00	1
Gentamicin IVI	0.24	0.24	3
Amoxicillin 875 mg oral	1.00	2.00	1
		3.00	1
Cloxacillin IVI 1 g	2.00	4.00	2

Ceftazidime IVI 1 g	4.00	2.00	2
Metronidazole Tablets	1.50	1.20	2
Amoxycillin Capsules	1.00	2.00	2
Clarithromycin Tablets	0.50	2.00	2
Co-Trimoxazole	1.92	0.96 1.92	1 1
Clindamycin IVI 600 mg	1.80	1.80	1
Cloxacillin Capsules	2.00	8.00	1
Ciprofloxacin Tablets	1.00	1.00	1
Cefepime IVI 2 g	2.00	6.00	1
Rifampicin IVI	0.60	0.60	1
Amikacin	1.00	0.75	1
Cefuroxime IVI	3.00	4.50	1
Cefazolin IVI	3.00	2.00	1

4.3.2 Microbiology Laboratory Test Data Review

When an infection was suspected, different types of specimens could be taken and sent to the NHLS Microbiology Laboratory to identify the pathogen using the Conventional Culture Method. If the patient had an open wound or an infected area, the specimen was commonly taken from that area. In Figure 12 and Figure 13, the pie charts show the different types of specimens that were taken and that isolated MRSA in the two wards.

4.3.2.1 Orthopaedic Ward

Within the orthopaedic ward, a total of 46 NHLS laboratory tests were conducted that isolated MRSA. Each patient had a range of one to ten with an average of three NHLS laboratory tests (based on the laboratory test number) that were conducted and that isolated MRSA.

Fluid, irrigation fluid and tissue specimens each isolated 12 out of the 46 MRSA results in the orthopaedic ward as shown in Figure 12.

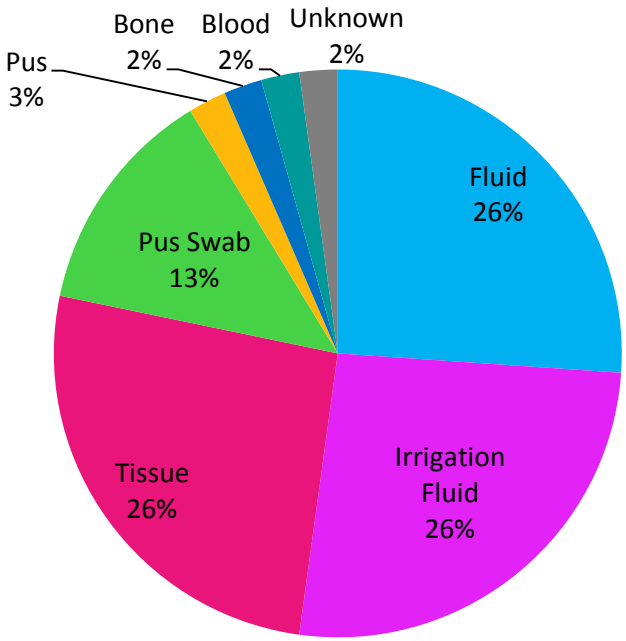


Figure 12: Types of Specimens Taken that Isolated MRSA in the Orthopaedic Ward in 2013

4.3.2.2 Vascular Ward

Within the vascular ward, a total of 45 NHLS laboratory tests were conducted that isolated MRSA. Each patient had a range of one to four with an average of two NHLS laboratory tests (based on the laboratory test number) that were conducted and that isolated MRSA.

From the 45 specimens that isolated MRSA in the vascular ward, 18 were from tissue, 14 were pus swabs and 7 were from pus as illustrated in Figure 13.

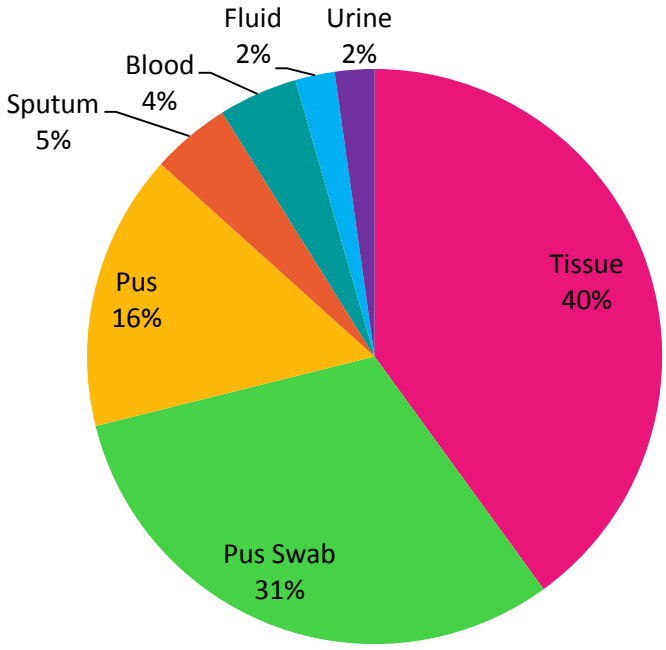


Figure 13: Types of Specimens Taken that Isolated MRSA in the Vascular Ward in 2013

4.4 Cost Analysis

4.4.1 Antibiotic Cost Calculations

The cost per antibiotic administered per patient in each ward is shown in Appendix 7 (Table 37 and Table 38). The summarised Tables of the sum of costs of the antibiotics administered per patient and the costs of the antibiotics per ward are shown below for each ward.

4.4.1.1 Orthopaedic Ward

The sum of the total utilization cost of antibiotics administered to each patient ranged from R307.18 to R11 926.85 with an average of R2 925.31 per patient. The sum of the daily cost of antibiotics administered to each patient ranged from R42.56 to R1 695.04 with an average of R408.42 per day as shown in Table 17.

Table 17: The Daily Cost and Total Utilization Cost of Antibiotics per Patient in the Orthopaedic Ward in 2013

Patient Number	Daily Cost (R)				Total Utilization Cost (R)
	Empiric	MRSA-Specific	Other	Total	
369P03	99.23	282.66	0.00	381.88	**2418.56**
369P09	116.74	0.00	0.00	116.74	**978.58**
369P12	145.71	1364.64	184.68	1695.04	**11926.85**
369P15	55.29	93.94	0.00	149.23	**1246.66**
369P06	107.23	48.66	368.33	524.22	**3851.81**
369P08	110.47	377.44	0.00	487.91	**4338.20**
369P13	97.42	0.00	0.00	97.42	**307.18**
369P14	173.59	0.00	0.00	173.59	**1431.67**
369P02	16.01	0.00	368.74	384.74	**2228.84**
369P04	18.74	95.63	0.00	114.38	**1201.56**
369P16	42.56	0.00	0.00	42.56	**470.36**
369P05	119.77	0.00	0.92	120.69	**1011.25**
369P10	132.52	375.74	0.00	508.26	**2512.50**
369P07	107.76	377.44	0.00	485.20	**2684.58**
369P01	95.76	95.63	0.00	191.39	**4209.32**
369P11	107.76	801.03	152.74	1061.53	**5987.08**
Total	**1546.57**	**3912.81**	**1075.40**	**6535.78**	**46804.99**
Average	**96.66**	**244.55**	**67.21**	**408.42**	**2925.31**

60% of the daily cost of antibiotics administered was for the MRSA-Specific Antibiotics administered and 24% of the daily cost of antibiotics administered was for Empiric Antibiotics.

Table 18: The Average Daily Cost, Number of Days and Total Utilization Cost per Antibiotic in the Orthopaedic Ward in 2013

Antibiotics	Average		
	Daily Cost (R)	Number of days	Total Utilization Cost (R)
Co-amoxiclav 625 mg Tablets	3.47	21	71.63
Co-amoxiclav 1 g Tablets	2.71	7	18.96
Co-amoxiclav 1.2 g IVI	37.56	5	187.80
Co-amoxiclav 0.6 g IVI	21.48	3	64.44
Gentamicin Irrigation System	95.76	14	1358.05
Rifampicin	1.59	12	20.35
Vancomycin Irrigation System	250.50	4	1033.30
Vancomycin IVI	115.29	9	1093.07
Cloxacillin Capsules	15.28	15	226.12
Cloxacillin IVI	34.09	5	180.92
Cefotaxime	184.68	9	1662.12
Cefazolin IVI	10.50	2	24.76
Linezolid	564.49	4	1975.72
Ertapenem IVI	368.33	4	1289.16
Metronidazole	0.41	7	2.85
Ciprofloxacin	0.92	32	29.37
Ceftazidime IVI	120.00	19	2279.93
Ceftazidime Irrigation System	32.74	1	32.74

As per Table 18, the average daily cost of the antibiotics administered ranged from R0.41 for metronidazole to R564.49 for linezolid. The average total utilization cost ranged from R2.85 for metronidazole for an average of seven days, to R2 279.93 for ceftazidime IVI for an average of 19 days.

4.4.1.2 Vascular Ward

The sum of the total utilization cost of antibiotics administered to each patient ranged from R8.00 to R15 092.31 with an average of R2 398.42 per patient. The sum of the daily cost of antibiotics administered to each patient ranged from R2.71 to R2 435.65 with an average of R462.51 per day as shown in Table 19.

Table 19: The Daily Cost and Total Utilization Cost of Antibiotics per Patient in the Vascular Ward in 2013

Patient Number	Daily Cost (R)				Total Utilization Cost (R)
	Empiric	MRSA-Specific	Other	Total	
395P02	480.00	187.87	1767.77	2435.65	15092.31
395P03	37.56	46.97	81.60	166.124	933.66
395P04	0.00	0.00	377.85	377.85	1511.40
395P05	37.56	0.00	504.86	542.42	4156.8
395P06	454.46	0.00	768.15	1222.62	5921.98
395P07	0.00	399.23	132.846	532.07	1439.20
395P08	240.00	0.00	0.00	240.00	1200.00
395P09	243.47	140.90	870.54	1254.91	8669.95
395P11	517.56	0.00	0.00	517.56	1830.24
395P12	2.71	0.00	0.00	2.71	51.45
395P13	37.56	0.00	0.92	38.48	233.62
395P14	0.00	0.00	232.50	232.50	1231.32
395P16	240.00	0.00	368.63	608.63	1809.55
395P17	37.56	0.00	0.00	37.56	225.36
395P18	82.98	93.94	0.00	176.91	1657.75
395P19	30.56	23.48	65.48	119.52	704.47
395P20	8.00	0.00	0.00	8.00	8.00
395P21	817.56	93.94	520.22	1431.72	6270.04
395P22	287.88	0.00	0.00	287.88	1055.16
395P23	480.00	0.00	61.53	541.53	3544.29
395P24	37.56	93.94	0.00	131.496	394.416
395P25	277.56	408.36	554.87	1240.786	3916.214
395P28	37.56	93.94	0.00	131.50	375.67
395P29	0.00	0.00	104.10	104.10	508.20
395P30	420.00	0.00	192.34	612.34	4381.70
395P31	4.06	0.00	0.00	4.06	16.25
395P32	50.08	0.00	0.00	50.08	1001.6
395P33	3.47	0.00	0.00	3.47	45.06
395P36	37.56	281.81	40.92	360.29	1368.58
Total	**4903.26**	**1864.36**	**6645.13**	**13412.76**	**69554.23**
Average	**169.08**	**64.29**	**229.14**	**462.51**	**2398.42**

Of the daily cost of antibiotics administered 14% was due to the MRSA-Specific Antibiotics administered and 37% of the daily cost of antibiotics administered was due to the Empiric Antibiotics.

Table 20: The Average Daily Cost, Number of Days and Total Utilization Cost per Antibiotic in the Vascular Ward in 2013

Antibiotics	Average		
	Daily Cost (R)	Number of days	Total Utilization Cost (R)
Piperacillin/tazobactam	214.74	6	1357.89
Co-amoxiclav IVI 1.2 g	38.45	6	259.34
Co-amoxiclav 625 mg Tablets	3.47	12	40.44
Co-amoxiclav 1 g Tablets	3.39	12	33.85
Vancomycin IVI 1 g	77.50	3	272.41
Ertapenem IVI 1 g	460.41	3	1289.16
Meropenem IVI 1 g	314.88	6	2099.17
Meropenem IVI 500 mg	191.58	6	1085.62
Imipenem IVI 1 g	250.93	3	815.53
Clindamycin IVI 600 mg	31.46	17	534.89
Cloxacillin IVI 1 g	41.95	9	356.59
Cloxacillin Capsules	30.56	3	91.67
Ciprofloxacin IVI	310.90	7	1575.23
Ciprofloxacin Tablets	0.92	9	8.26
Ceftazidime IVI 1 g	65.48	8	491.10
Cefepime IVI 1 g	45.01	5	233.24
Cefepime IVI 2 g	116.73	5	583.65
Metronidazole Tablets	0.30	3	0.91
Metronidazole IVI	16.12	7	104.75
Gentamicin IVI	47.88	4	207.48
Amoxicillin Capsules	0.82	7	5.71
Clarithromycin Tablets	7.68	4	26.87
Rifampicin IVI	314.42	3	943.26
Amikacin	20.61	1	20.61
Cefuroxime IVI	47.06	3	141.18
Cefazolin IVI	8.00	1	8.00
Co-trimoxazole	0.38	4	1.90

As per Table 20, the average daily cost of the antibiotics administered ranged from R0.30 for metronidazole tablets to R460.41 for ertapenem IVI. The average total utilization cost ranged from R0.91 for metronidazole tablets for an average of three days, to R2 099.17 for meropenem IVI 1g for an average of six days.

4.4.2 NHLS Laboratory Test Cost Calculations

The sum of all the laboratory tests conducted per patient was calculated and is shown in the tables below. Appendix 7 (Table 39 and Table 40) provides details of the cost per laboratory test per patient.

4.4.2.1 Orthopaedic Ward

In the orthopaedic ward, the cost per NHLS laboratory test that isolated MRSA ranged from R118.38 to R592.80 with an average of R335.09 per test. Each laboratory test had only one microscopy step and the cost of the microscopy step was a standard cost of R36.93 with the exception of one code which was R38.41. The Culture and Sensitivity Cost varied between R81.45 and R555.87 per laboratory test, as a combination of different Culture and Sensitivity steps were conducted per laboratory test. The detailed laboratory steps and costing information was not available for one patient (369P14).

As some patients had more than one laboratory test conducted that isolated MRSA, the sum of the laboratory tests was calculated for each patient to obtain the total cost of laboratory tests per patient, as displayed in Table 21. The total cost of laboratory tests that isolated MRSA per patient ranged from R260.13 to R3184.23 with an average of R921.51 per patient.

Table 21: The Microscopy, Culture and Sensitivity and Total Costs of the NHLS Laboratory Tests conducted that isolated MRSA per patient in the Orthopaedic Ward in 2013

Patient Number	Cost (R)		Total Price (R)
	Microscopy	Culture and Sensitivity	
369P03	221.58	1443.46	1665.04
369P09	73.86	538.25	612.11
369P12	73.86	582.44	656.30
369P15	36.93	223.20	260.13
369P06	73.86	574.60	648.46
369P08	258.51	2707.40	2965.91
369P13	36.93	223.20	260.13

369P14	0.00	0.00	0.00
369P02	36.93	223.20	260.13
369P04	36.93	223.20	260.13
369P16	38.41	232.13	270.54
369P05	73.86	731.50	805.36
369P10	73.86	504.24	578.10
369P07	73.86	618.78	692.64
369P01	369.30	2814.93	3184.23
369P11	147.72	1477.19	1624.91
Total	**1626.40**	**13117.72**	**14744.12**
Average per Patient	**101.65**	**819.86**	**921.51**
Average per Test	**36.96**	**298.13**	**335.09**

4.4.2.2 Vascular Ward

In the vascular ward, the cost per NHLS laboratory test that isolated MRSA ranged from R168.37 to R660.40 with an average of R373.03 per test. Each laboratory test had only one microscopy step and the cost of the microscopy step was either R36.93 or R38.41. The Culture and Sensitivity Cost varied between R131.44 and R623.47 per laboratory test, as a combination of different Culture and Sensitivity steps were conducted per laboratory test. The detailed laboratory steps and costing information was not available for one patient (395P33).

As some patients had more than one laboratory test conducted that isolated MRSA, the sum of the laboratory tests was calculated for each patient to obtain the total cost of laboratory test per patient and is displayed in the Table 22. The total cost of laboratory test per patient ranged from R168.37 to R1 492.05 with an average of R565.97 per patient.

Table 22: The Microscopy, Culture and Sensitivity and Total Costs of the NHLS Laboratory Tests that isolated MRSA per patient in the Vascular Ward in 2013

Patient Number	Cost (R)		Total Price (R)
	Microscopy	Culture and Sensitivity	
395P02	73.86	1033.01	1106.87
395P03	73.86	632.44	706.30
395P04	36.93	223.2	260.13
395P05	36.93	532.04	568.97
395P06	110.79	787.19	897.98

395P07	76.82	545.59	622.41
395P08	36.93	592.08	629.01
395P09	36.93	223.2	260.13
395P11	36.93	131.44	168.37
395P12	36.93	223.2	260.13
395P13	73.86	446.4	520.26
395P14	152.16	1339.89	1492.05
395P16	73.86	903.84	977.70
395P17	38.41	341.84	380.25
395P18	73.86	663.48	737.34
395P19	36.93	247.03	283.96
395P20	73.86	606.27	680.13
395P21	73.86	658.61	732.47
395P22	36.93	479.38	516.31
395P23	36.93	223.2	260.13
395P24	36.93	510.64	547.57
395P25	73.86	639.66	713.52
395P28	36.93	223.2	260.13
395P29	38.41	232.13	270.54
395P30	73.86	589.65	663.51
395P31	36.93	579.7	616.63
395P32	38.41	354.96	393.37
395P33	0.00	0.00	0.00
395P36	73.86	813.08	886.94
Total	**1636.76**	**14776.35**	**16413.11**
Average per Patient	**56.44**	**509.53**	**565.97**
Average per Test	**37.20**	**335.83**	**373.03**

4.4.3 Antibiotic Utilization plus NHLS Laboratory Tests Cost Calculation

For each patient the total cost of Antibiotics administered plus NHLS laboratory tests conducted was calculated and is presented in Appendix 7 (Table 41 and Table 42).

4.4.3.1 Orthopaedic Ward

Cost Calculations of Antibiotic Utilization plus NHLS Laboratory Tests per Patient in the Orthopaedic Ward in 2013 were performed. The total sum of the Antibiotic Utilization Cost and total NHLS cost per patient in the orthopaedic ward ranged from R567.31 to R12 583.15 as illustrated in Figure 14.

4.4.3.2 Vascular Ward

Cost Calculations of Antibiotic Utilization plus NHLS Laboratory Tests per Patient in the Vascular Ward in 2013 were performed. The total sum of the Antibiotic Utilization Cost and total NHLS cost per patient in the vascular ward ranged from R45.06 to R16 199.18 as illustrated in Figure 15.

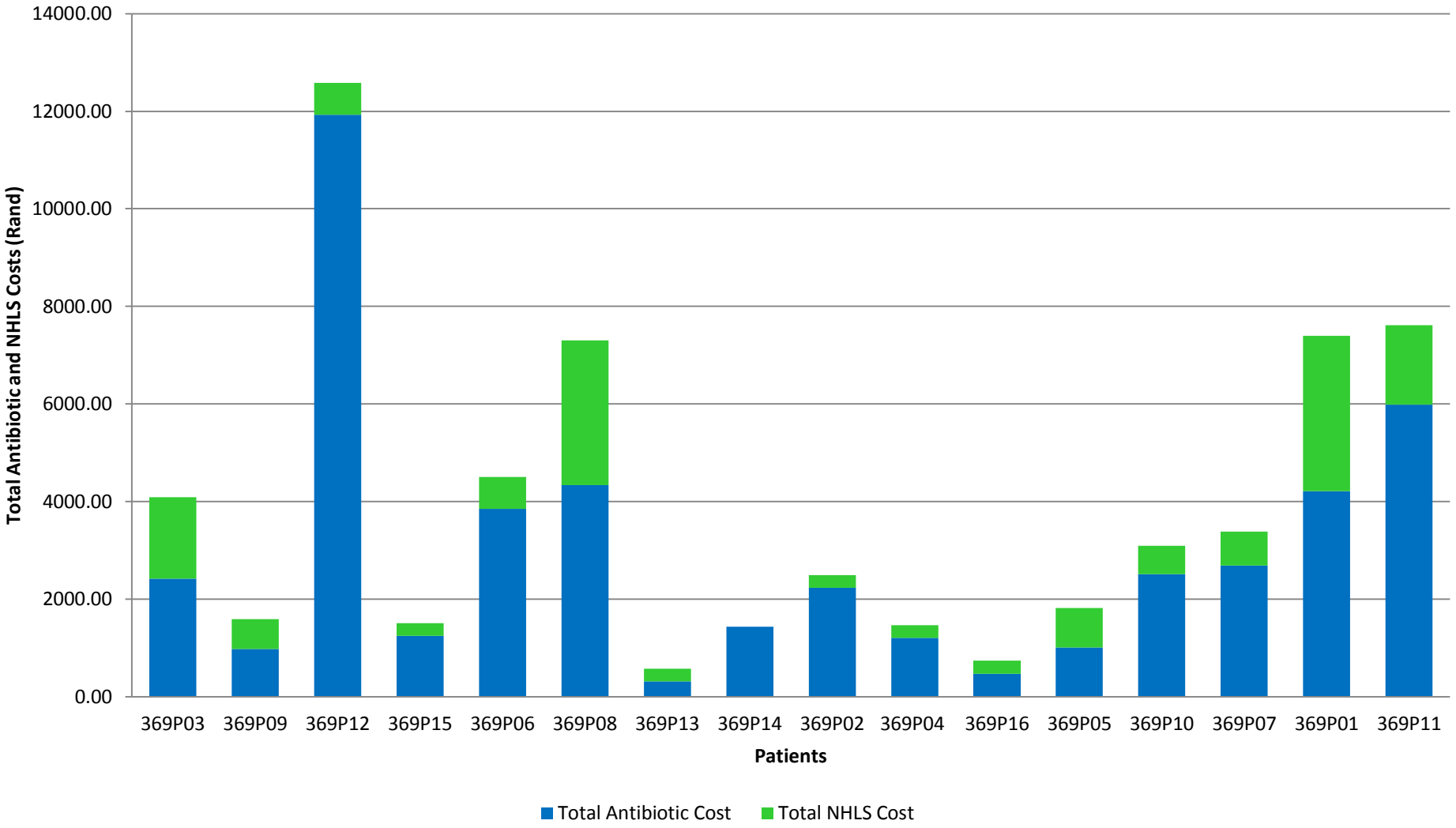


Figure 14: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted per Patient in the Orthopaedic Ward in 2013

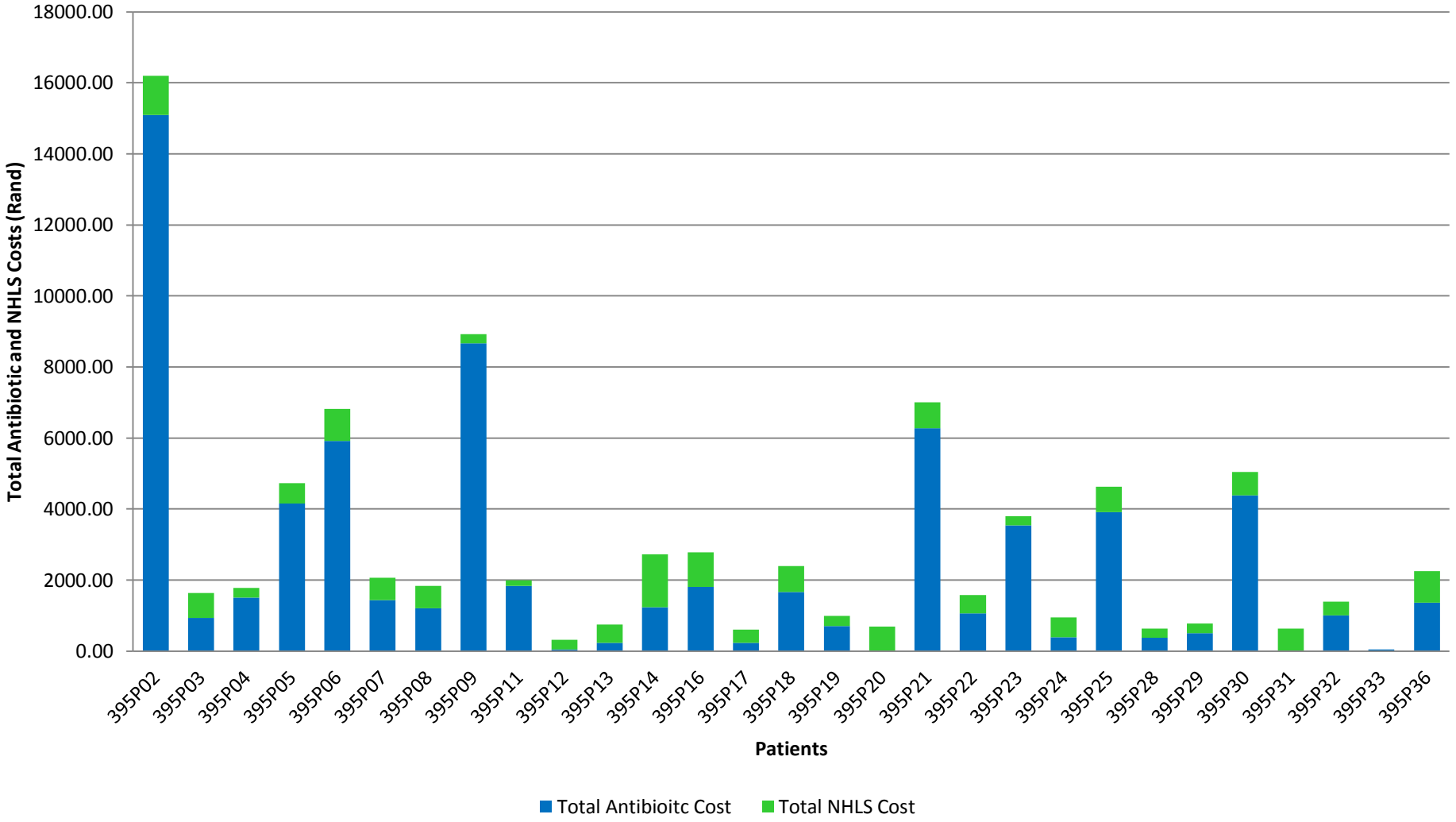


Figure 15: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted per Patient in the Vascular Ward in 2013

4.5 Decision-Tree-Analytic Models

Two decision-tree-analytic models were developed depicting the various management pathways of patients with a suspected infection, one for the orthopaedic ward and one for the vascular ward. Once the structures of these decision-tree-analytic models were complete, numeric values were entered into the tree as variables, probabilities and payoffs. The two decision-tree-analytic models were first run using the actual probabilities that occurred in the clinical setting in each ward and are referred to as the "actual decision-tree-analytic models". The two decision-tree-analytic models were then run by using variables to allocate equal probabilities to each branch for each ward and are referred to the "equal decision-tree-analytic models".

4.5.1 Decision-Tree-Analytic Model Structure and Parameters

4.5.1.1 Variables

Separate variables were created for each ward as the costs and probabilities differed. Variables starting with the prefix "c" were variables denoting the cost of antibiotics or testing methods and variables starting with the prefix "p" were variables denoting the probability of an event occurring. These variables are described in Table 23 and Table 24.

Table 23: **Variables used in the Decision-Tree-Analytic Models for the Orthopaedic Ward**

Name	Description	Root Definition	Low Value	High Value
cSpecimenM	Cost of Specimen Sent for Microscopy	R101.65	2.16	201.14
cSpecimenCS	Cost of Specimen Sent for Culture and Sensitivity	R819.86	0.00	1682.00
cDailyMrsaSpecificAntibiotic	Average cost of MRSA-Specific Antibiotic per patient per day	R244.55	0.00	617.15
cDailyEmpiricAntibiotic	Average cost of Empiric Antibiotic per patient per day	R96.66	53.21	140.11
cDailyOtherAntibiotic	Average cost of Other Antibiotics per patient per day	R67.21	0.00	198.05
cXpertMRSA	Cost of 1 Xpert MRSA Kit	R307.52	153.76	461.28
pEmpiricAntibiotics	Probability of Receiving Empiric Antibiotics	0.50	0.00	1.00
pMrsaSpecificAntibiotics	Probability of Receiving MRSA-Specific Antibiotics	0.50	0.00	1.00
pMrsaIsolated	Probability of MRSA Isolated	0.50	0.00	1.00
pSpecimenSentMCS	Probability of a Specimen being Sent for MCS	0.50	0.00	1.00
pConfirmationByCS	Probability of Confirmation of MRSA by Culture and Sensitivity	0.50	0.00	1.00
pXpertMRSA	Probability of Xpert MRSA test	0.50	0.00	1.00
pOtherAntibiotics	Probability of Receiving Other Antibiotics	0.50	0.00	1.00

Table 24: Variables used in the Decision-Tree-Analytic Models for the Vascular Ward

Name	Description	Root Definition	Low Value	High Value
CSpecimenM	Cost of Specimen Sent for Microscopy	R56.44	26.98	85.90
cSpecimenCS	Cost of Specimen Sent for Culture and Sensitivity	R509.53	216.10	802.96
cDailyMrsaSpecificAntibiotic	Average cost of MRSA-Specific Antibiotic per patient per day	R64.29	0.00	180.62
cDailyEmpiricAntibiotic	Average cost of Empiric Antibiotic per patient per day	R169.08	0.00	385.02
cDailyOtherAntibiotic	Average cost of Other Antibiotics per patient per day	R229.14	0.00	616.36
cXpertMRSA	Cost of 1 Xpert MRSA Kit	R307.52	153.76	461.28
pEmpiricAntibiotics	Probability of Receiving Empiric Antibiotics	0.50	0.00	1.00
pMrsaSpecificAntibiotics	Probability of Receiving MRSA-Specific Antibiotics	0.33	0.17	0.50
pMrsaIsolated	Probability of MRSA Isolated	0.50	0.00	1.00
pSpecimenSentMCS	Probability of a Specimen being Sent for MCS	0.50	0.00	1.00
pConfirmationByCS	Probability of Confirmation of MRSA by Culture and Sensitivity	0.50	0.00	1.00
pXpertMRSA	Probability of Xpert MRSA test	0.50	0.00	1.00
pOtherAntibiotics	Probability of Receiving Other Antibiotics	0.33	0.17	0.50

4.5.1.2 Complete Decision-Tree-Analytic Models

For each ward the completed decision-tree-analytic models with the variables, probabilities and payoffs are shown, first with their actual probabilities and then with the variables for equal probabilities. Figure 16 and Figure 17 represent the decision-tree-analytic models for the orthopaedic ward followed by Figure 18 and Figure 19 which represent the decision-tree-analytic models for the vascular ward

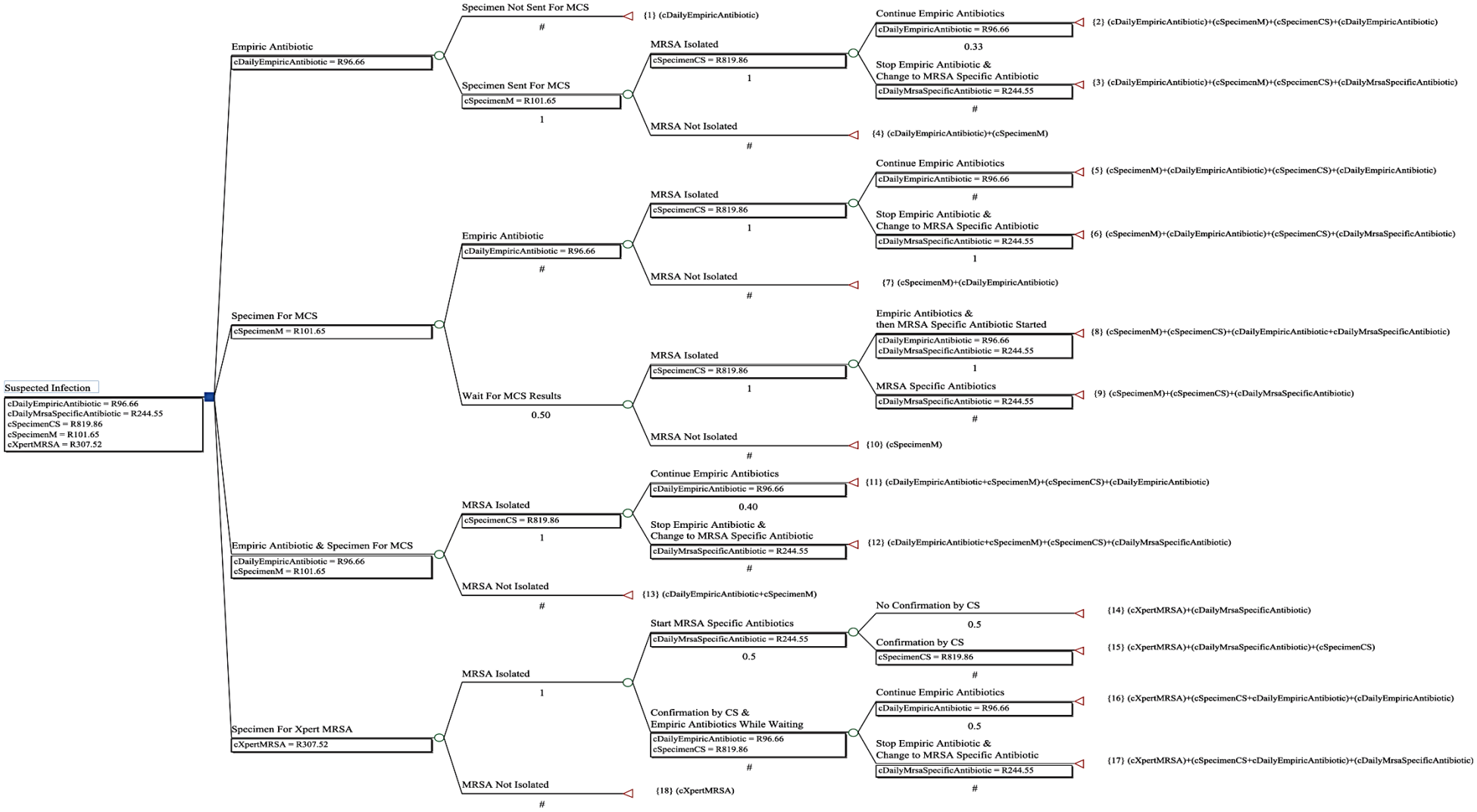


Figure 16: Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward

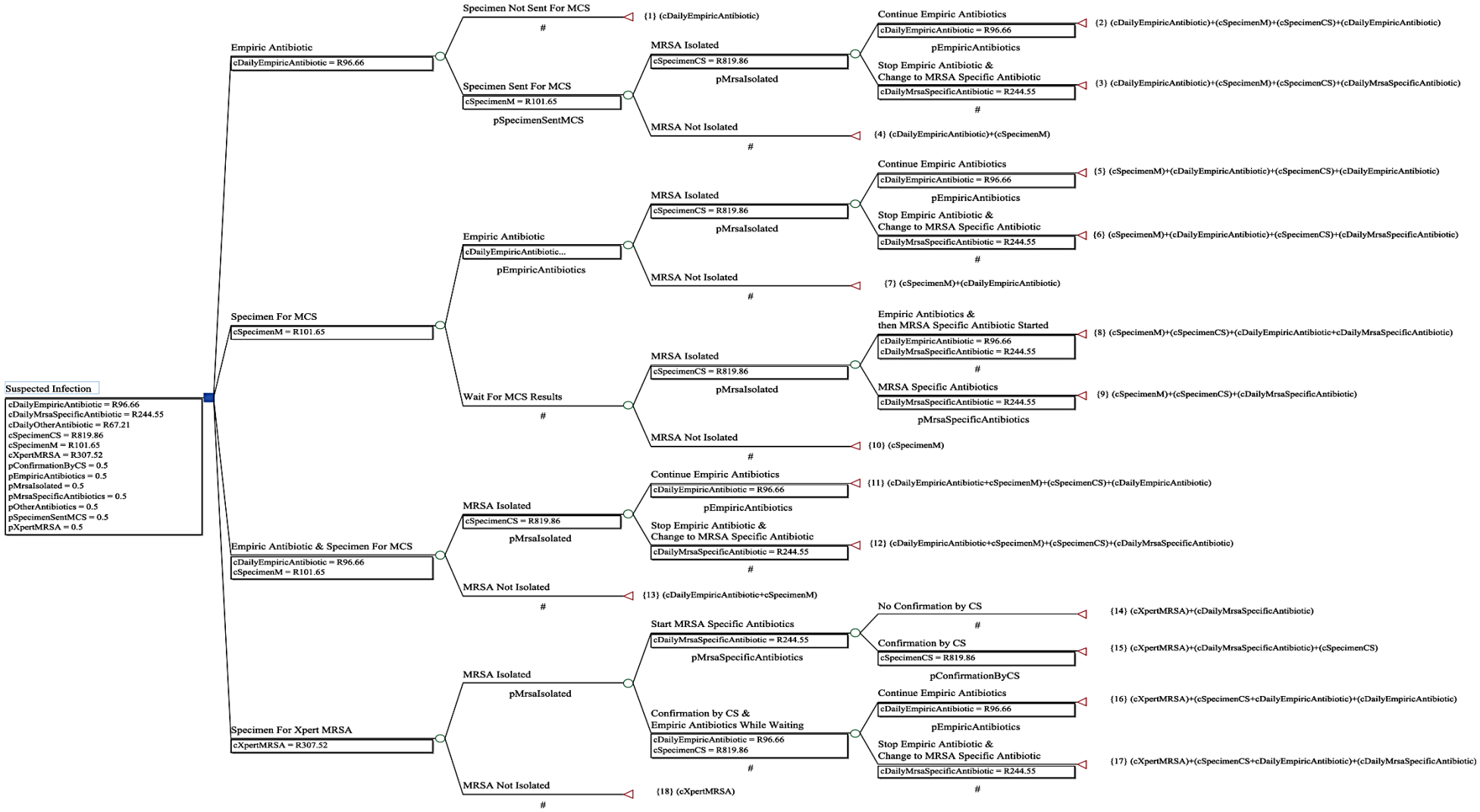


Figure 17: Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward

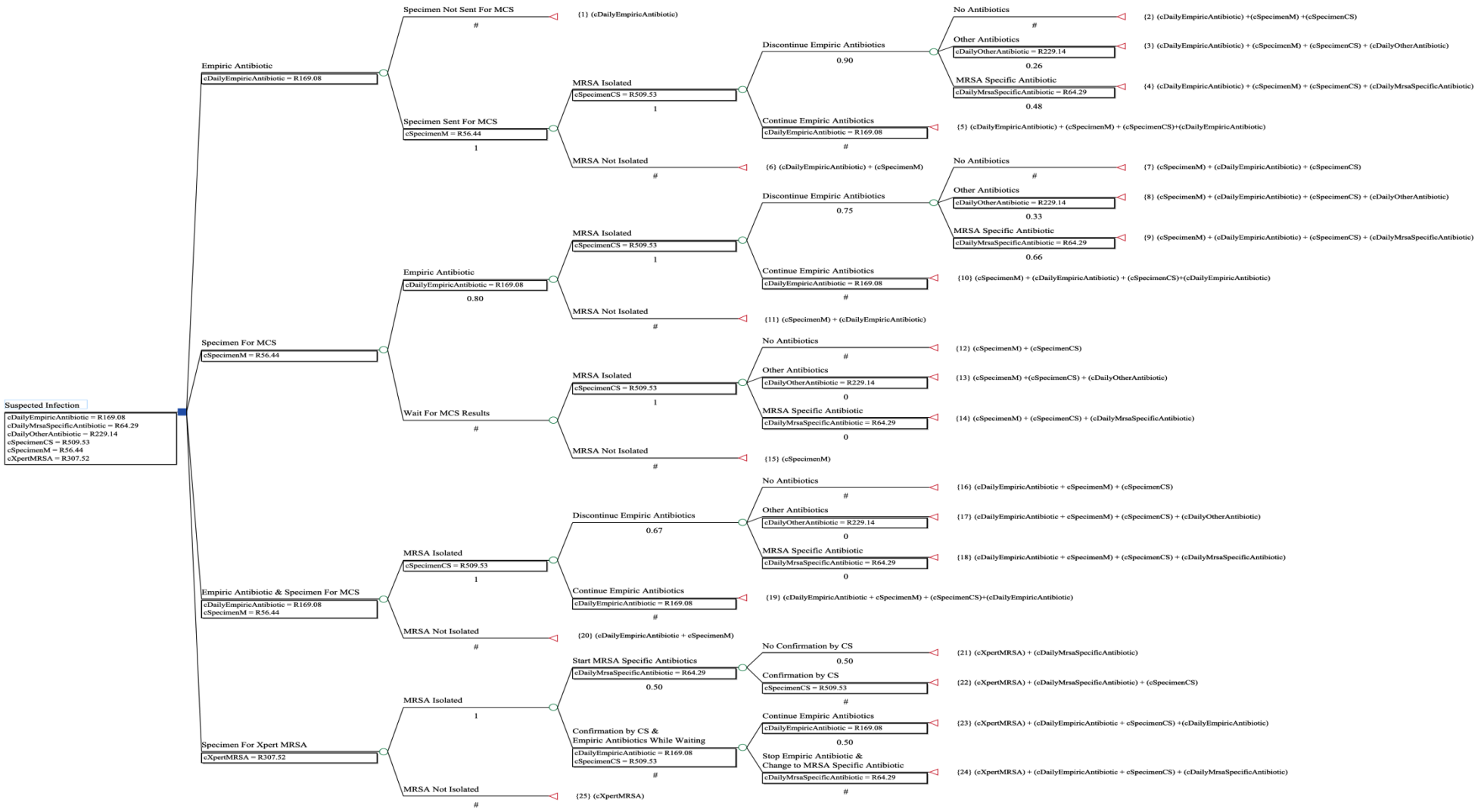


Figure 18: Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward

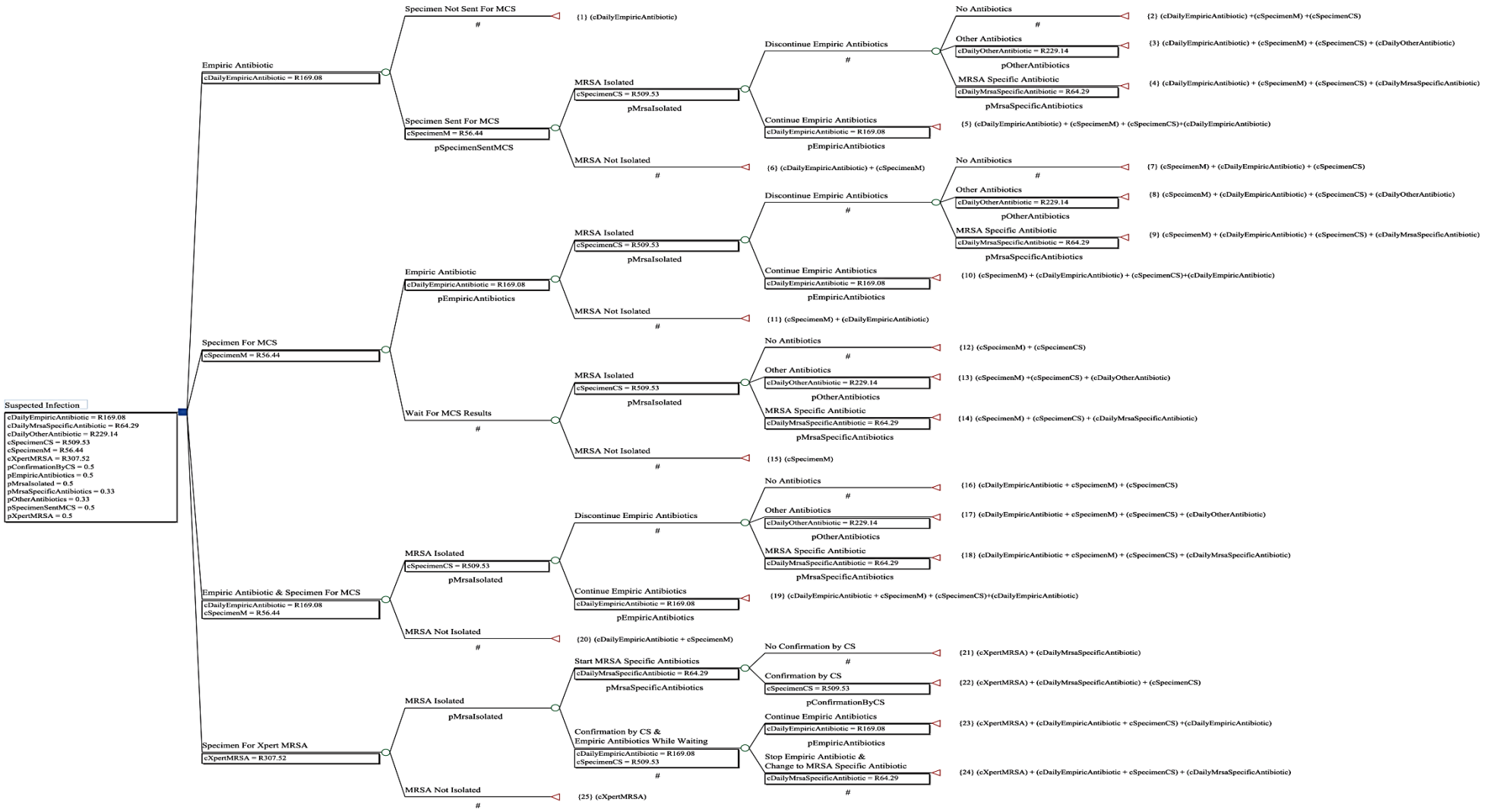


Figure 19: **Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward**

4.5.2 Analysis of the Decision-Tree-Analytic Models

The decision-tree-analytic models generated when Rollback was run showing the Rankings, Path Probabilities and Payoff are illustrated in Appendix 8 (Figure 37, Figure 38, Figure 39 and Figure 40).

4.5.2.1 Rankings

Table 25 compares the rankings of the strategies for the two decision-tree-analytic models when Rollback was run with the actual and equal probabilities in the orthopaedic and vascular ward.

Table 25: Rankings for the Decision-Tree-Analytic Models run with Actual and then Equal Probabilities in the Orthopaedic and Vascular Ward

Strategy	Orthopaedic (R)		Vascular (R)	
	Actual	Equal	Actual	Equal
Empiric Antibiotic	1 213.92	395.10	833.35	357.92
Specimen For MCS	1 262.72	675.78	805.88	453.19
Empiric Antibiotic & Specimen For MCS	1 203.56	693.54	790.85	546.76
Specimen For Xpert MRSA	**1 178.32**	742.92	864.69	626.59

In the current clinical setting in the orthopaedic ward, the optimal strategy was when Empiric Antibiotics were administered and Specimen For MCS was taken at the same time. However, if the Xpert MRSA tests were to be implemented in this current setting in the orthopaedic ward, the optimal strategy would be to first take a Specimen For Xpert MRSA testing. When equal probabilities were assigned to the orthopaedic ward, the optimal strategy was to first administer Empiric Antibiotics.

As in the current clinical setting in the orthopaedic ward, the optimal strategy in the current clinical setting in the vascular ward was also when Empiric Antibiotics were administered and a Specimen For MCS was taken at the same time. If the Xpert MRSA tests were to be implemented in this current setting in the vascular ward, the strategy of sending a Specimen For Xpert MRSA testing was the most expensive strategy. When equal probabilities were assigned to the vascular ward, the optimal strategy was also to first administer Empiric Antibiotics.

4.5.2.2 Payoffs and Path Probabilities

The payoff's expected value and the path probability for each individual branch in each tree were calculated and are displayed in Table 26 and Table 27. The expected value represents the total cost of a single management pathway for a patient with a suspected infection and

the path probability represents the chance of that pathway occurring. For each branch, the payoff's expected value was the same for the actual decision-tree-analytic models and for the equal decision-tree-analytic models, however, the path probabilities differed. The terminal nodes for each branch were numbered as scenario numbers, with scenario number one being the pathway to the end of the first top branch, scenario number two being the branch below that, until scenario 18, being the last bottom branch in the orthopaedic tree and scenario 25 being the last bottom branch in the vascular tree.

Table 26: The Expected Value of the Payoffs and the Path Probabilities for the Decision-Tree-Analytic Models in the Orthopaedic Ward

Scenario Number	Expected Value (R)	Path Probability	
		Actual	Equal
1	96.66	0.00	0.50
2	1 114.83	0.33	0.12
3	1 262.72	0.67	0.12
4	198.31	0.00	0.25
5	1 114.83	0.00	0.12
6	1 262.72	0.50	0.12
7	198.31	0.00	0.25
8	1 262.72	0.50	0.12
9	1 166.06	0.00	0.12
10	101.65	0.00	0.25
11	1 114.83	0.40	0.25
12	1 262.72	0.60	0.25
13	198.31	0.00	0.50
14	552.07	0.25	0.12
15	1 371.93	0.25	0.12
16	1 320.70	0.25	0.12
17	1 468.59	0.25	0.12
18	307.52	0.00	0.50

The total value (expected value of a payoff) for a management pathway for a patient with a suspected infection in the orthopaedic ward ranged from R96.66 to R1 468.59. However, the pathway costing R96.66 had an actual probability of zero thus indicating that it did not occur in clinical practice. The pathway with the highest probability in the actual decision-tree-analytic model had an expected value of R1 262.72.

Table 27: The Expected Value of the Payoffs and the Path Probabilities for the Decision-Tree-Analytic Models in the Vascular Ward

Scenario Number	Expected Value (R)	Path Probability	
		Actual	Equal
1	169.08	0.00	0.50
2	735.05	0.23	0.04
3	964.19	0.23	0.04
4	799.34	0.43	0.04
5	904.13	0.10	0.12
6	225.52	0.00	0.25
7	735.05	0.01	0.04
8	964.19	0.20	0.04
9	799.34	0.40	0.04
10	904.13	0.20	0.12
11	225.52	0.00	0.25
12	565.97	0.20	0.08
13	795.11	0.00	0.08
14	630.26	0.00	0.08
15	56.44	0.00	0.25
16	735.05	0.67	0.08
17	964.19	0.00	0.08
18	799.34	0.00	0.08
19	904.13	0.33	0.25
20	225.52	0.00	0.50
21	371.81	0.25	0.08
22	881.34	0.25	0.08
23	1 155.21	0.25	0.17
24	1 050.42	0.25	0.17
25	307.52	0.00	0.50

In the vascular ward, the total value (expected value of a payoff) for a management pathway for a patient with a suspected infection ranged from R56.44 to R1 155.21. The pathway which had the expected value of R56.44 had an actual path probability of zero, thus indicating that this did not occur in clinical practice. The pathway with the highest probability in the actual decision-tree-analytic model had an expected value of R735.05.

4.5.2.3 Sensitivity and Threshold Analysis

One-way sensitivity analyses were performed for each variable in each decision-tree-analytic models. The Sensitivity Analysis Graphs along with threshold reports were interpreted. Only those Sensitivity Analysis Graphs which showed a change in the optimal strategy are discussed and shown in Figure 20 to Figure 32 below.

As all of the sensitivity analyses were performed from the decision node, each line on the one-way sensitivity analysis graph represented one of the strategies that emitted from the decision node. However, when two of the strategies had the same expected value, then these two lines were superimposed and appeared as one line on the graph. For each variable selected, the one-way sensitivity analysis graph showed the Expected Values of the strategies on the y-axis and the range (low to high value) of the selected variable on the x-axis. The x-axis was labelled according to the description of the selected variable. The points plotted on the graph were a function of each strategy's expected value when increasing the cost of the selected variable.

A threshold occurs when two lines in the sensitivity analysis graph cross over and causes the optimal strategy to change. Thresholds are indicated on the Sensitivity Analysis graphs shown below by a grey vertical dotted line and further details of the thresholds are reported in the Threshold Tables in Appendix 9 (Table 43, Table 44, Table 45, Table 46). The Variable Value is the value of the variable at the point at which the Threshold is reached. The Expected Value represents the equal Expected Value of Strategy 1 and Strategy 2 at the Threshold.

4.5.2.3.1 One-Way Sensitivity Analyses Performed for the Variables in the Decision-Tree-Analytic Models in the Orthopaedic Ward

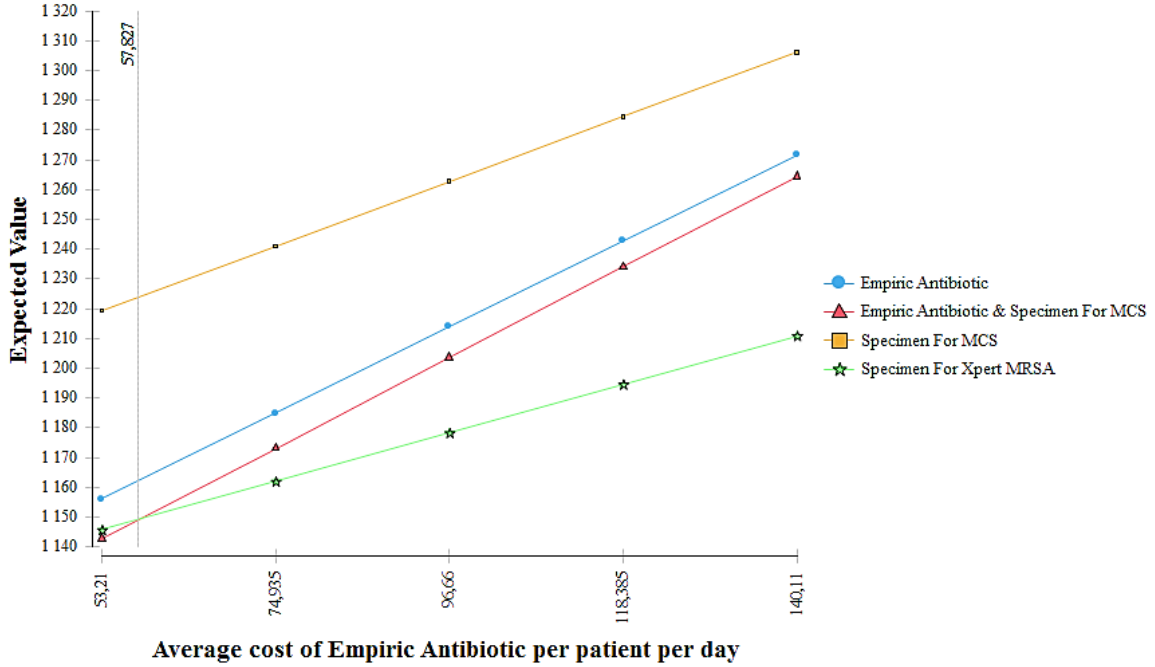


Figure 20: One-Way Sensitivity Analysis Graph for the Variable cDailyEmpiricAntibiotic in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward

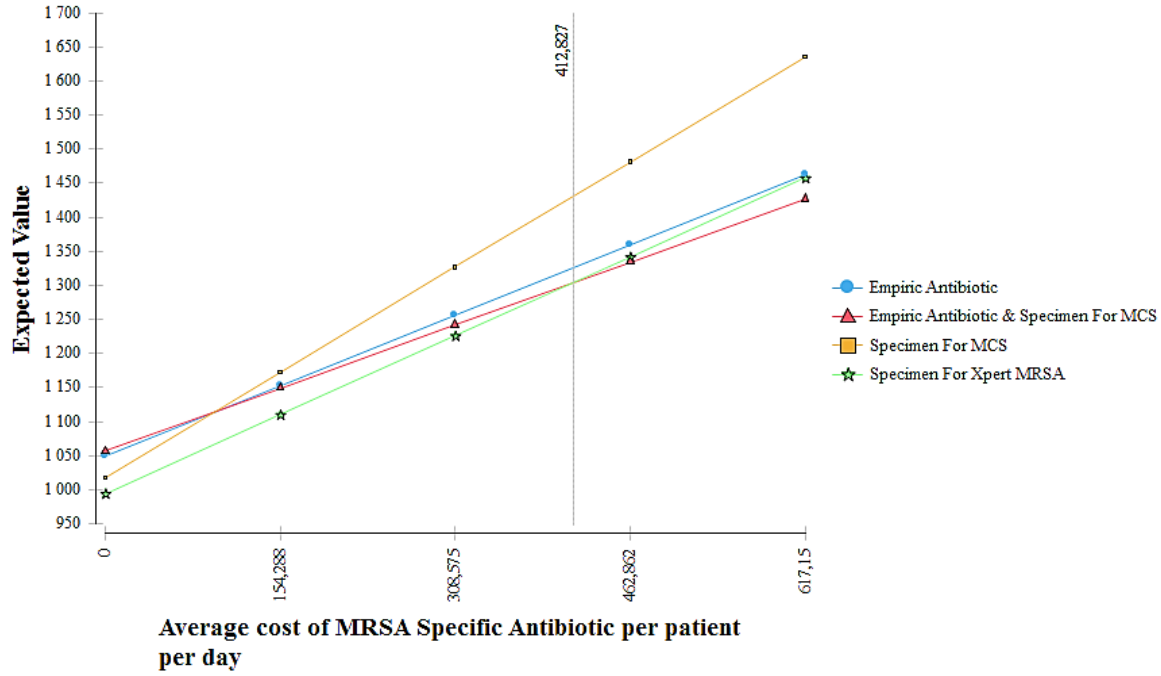


Figure 21: One-Way Sensitivity Analysis Graph for the Variable cDailyMrsaSpecificAntibiotic in the Actual Decision-Tree-Analytic model in the Orthopaedic Ward

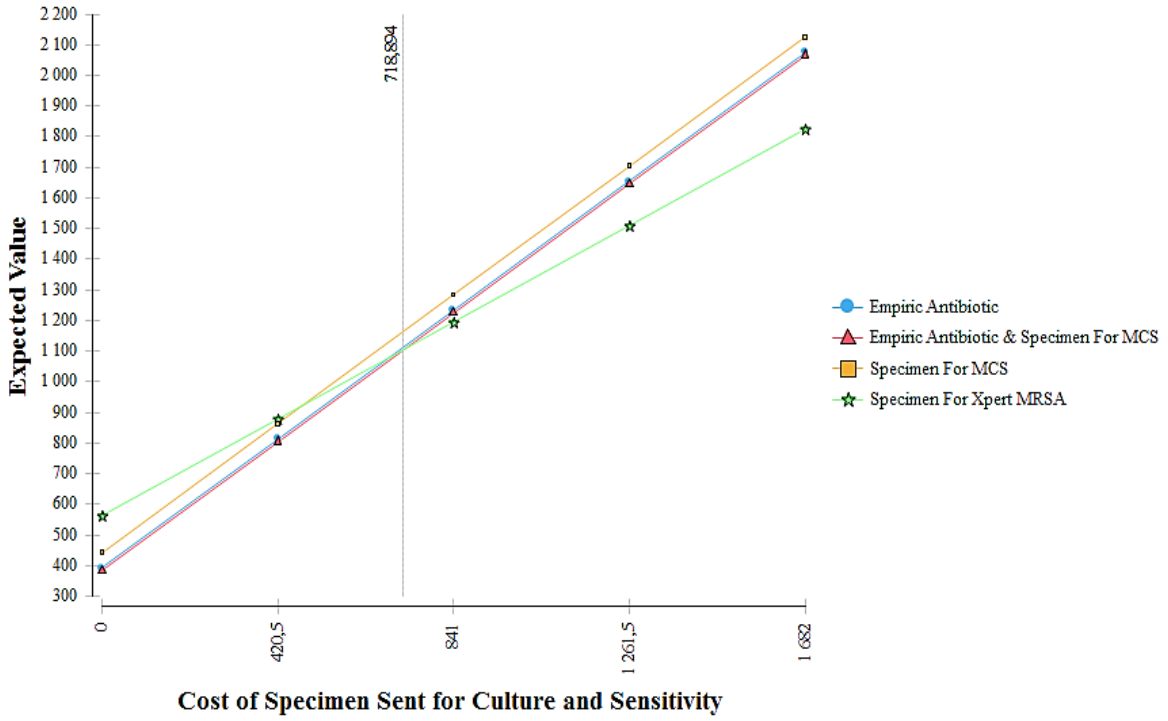


Figure 22: One-Way Sensitivity Analysis Graph for the Variable cSpecimenCS in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward

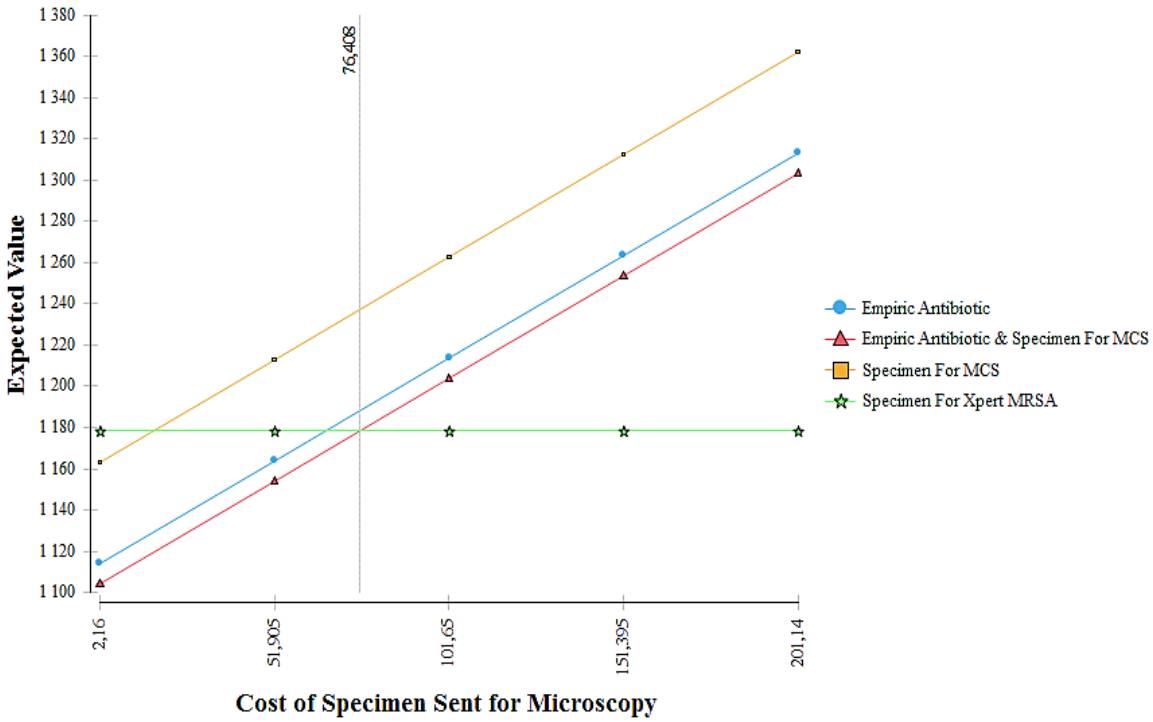


Figure 23: One-Way Sensitivity Analysis Graph for the Variable cSpecimenM in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward

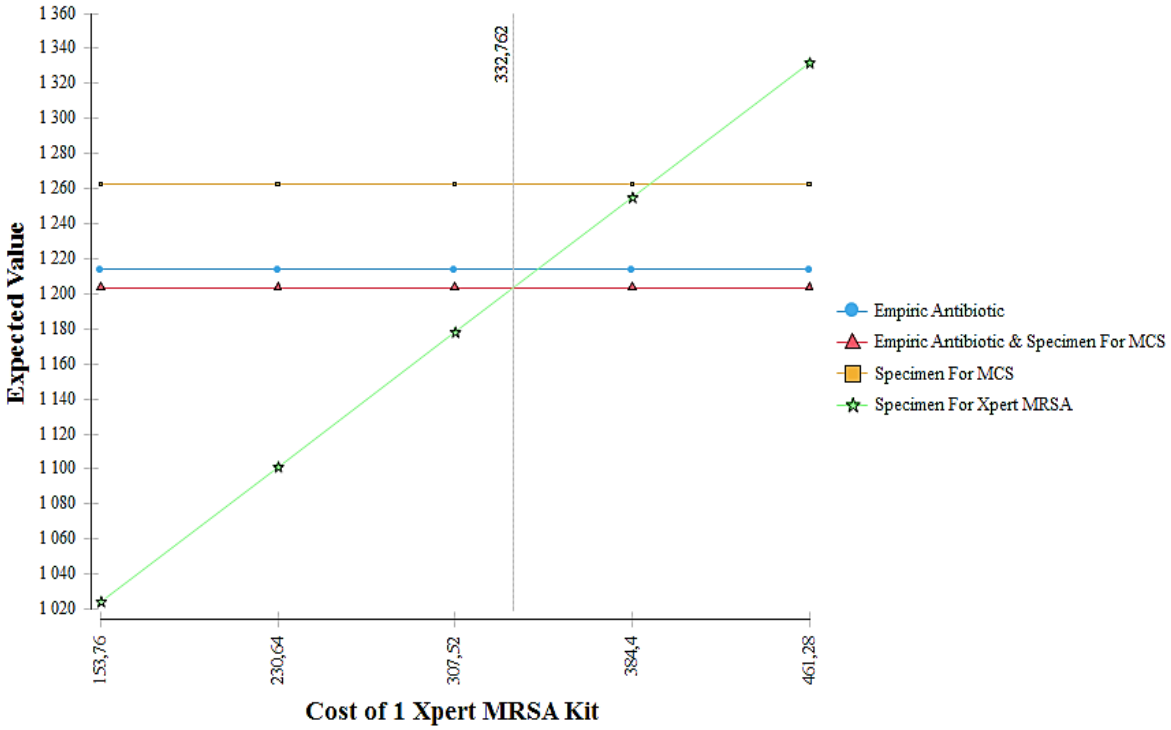


Figure 24: One-Way Sensitivity Analysis Graph for the Variable cXpertMRSA in the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward

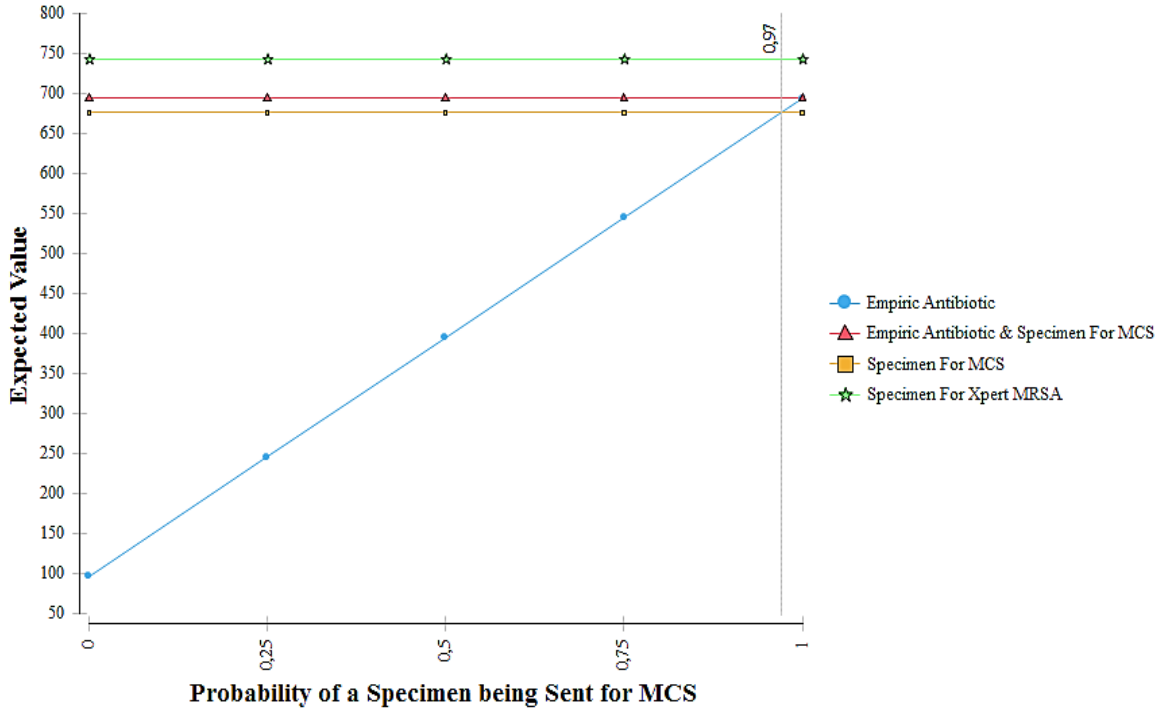


Figure 25: One-Way Sensitivity Analysis Graph for the Variable pSpecimenSentMCS in the Equal Decision-Tree-Analytic Model in the Orthopaedic Ward

For the variable cSpecimenM, the expected values of three strategies of Empiric Antibiotic, Empiric Antibiotic & Specimen For MCS and Specimen For MCS, increased as the cost of the variable increased and thus indicated that all three strategies were sensitive to this variable in both the actual and equal decision-tree-analytic models. However, all four strategies were sensitive to variables cSpecimenCS, cDailyMrsaSpecificAntibiotic and cDailyEmpiricAntibiotic, as all of the lines in these sensitivity analysis graphs deviated from the horizontal in both the actual and equal decision-tree-analytic models.

The expected values of the strategy of Specimen For Xpert MRSA testing were represented as an increasing function of the variable cXpertMRSA and were thus sensitive to the Cost of One Xpert MRSA Kit. The remaining three strategies of Empiric Antibiotic, Specimen For MCS and Empiric Antibiotic & Specimen For MCS, appeared as horizontal lines with no increase and were thus not sensitive to the variable cXpertMRSA. This was true for both situations using the actual and the equal probabilities in the orthopaedic ward.

Regarding the sensitivity analysis conducted for variables representing the equal probabilities in the orthopaedic ward, the following could be deduced. The decision-tree-analytic model was sensitive to the probability of MRSA isolated, as the expected values of all four strategies increased as the probability of isolating MRSA increased. The expected value of all four strategies also changed as the variable pEmpiricAntibiotics increased, thus showing that the decision-tree-analytic model was sensitive to the probability of receiving antibiotics. For the variable pConfirmationByCS, only the expected values of the Specimen For Xpert MRSA strategy increased as the probability of confirmation by culture and sensitivity increased and for the variable pSpecimenSentMCS, only the expected value of the Empiric Antibiotic Strategy increased as the probability of a specimen being sent for MCS increased. The strategies Specimen For MCS and Specimen For Xpert MRSA were sensitive to the variable pMrsaSpecificAntibiotics as their expected values increased as the probability of receiving MRSA-Specific Antibiotics increased.

4.5.2.3.2 One-Way Sensitivity Analyses Performed for the Variables in the Decision-Tree-Analytic Models in the Vascular Ward

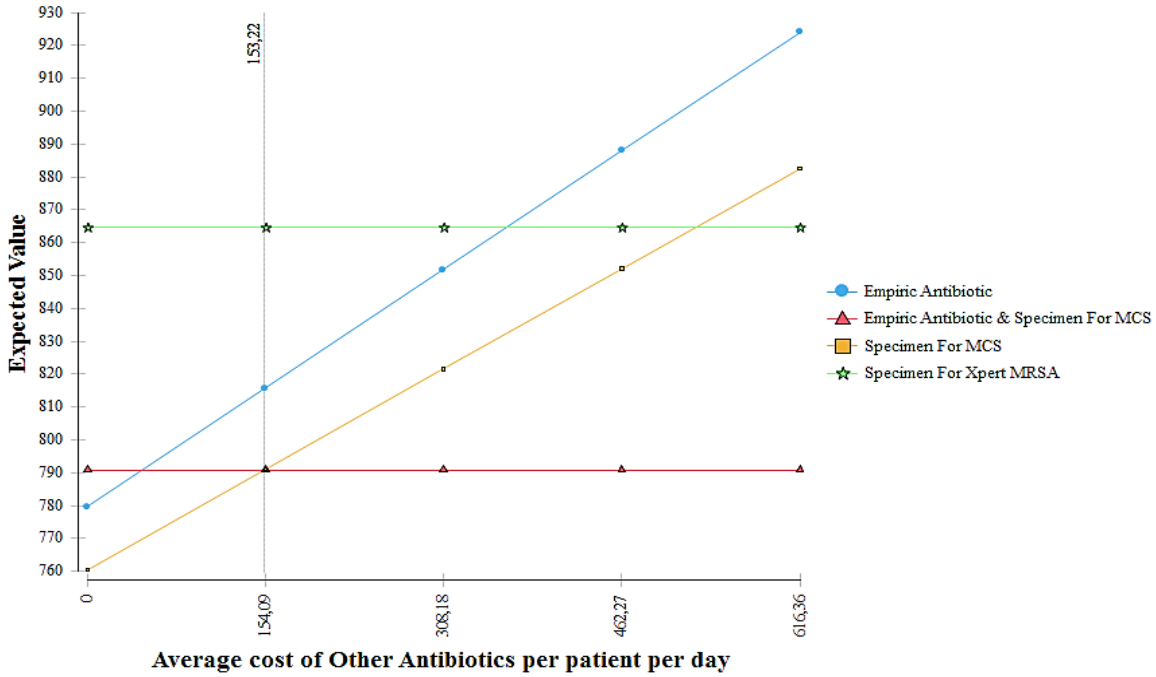


Figure 26: One-Way Sensitivity Analysis Graph for the Variable cDailyOtherAntibiotic in the Actual Decision-Tree-Analytic Model in the Vascular Ward

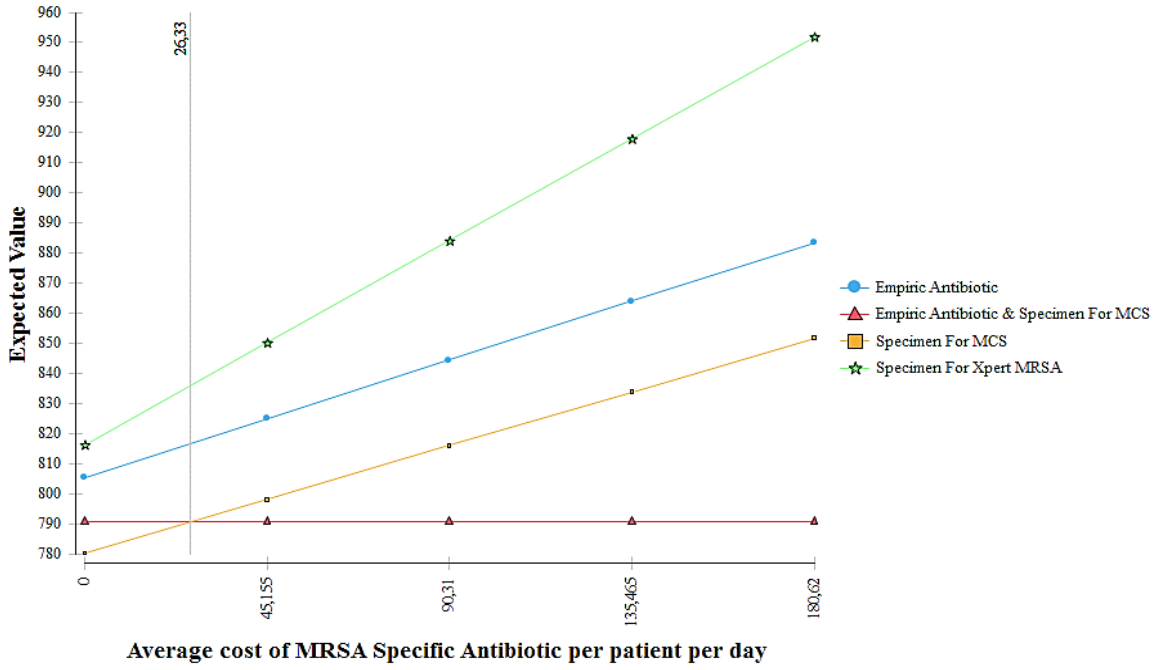


Figure 27: One-Way Sensitivity Analysis Graph for the Variable cDailyMrsaSpecificAntibiotic in the Actual Decision-Tree-Analytic Model in the Vascular Ward

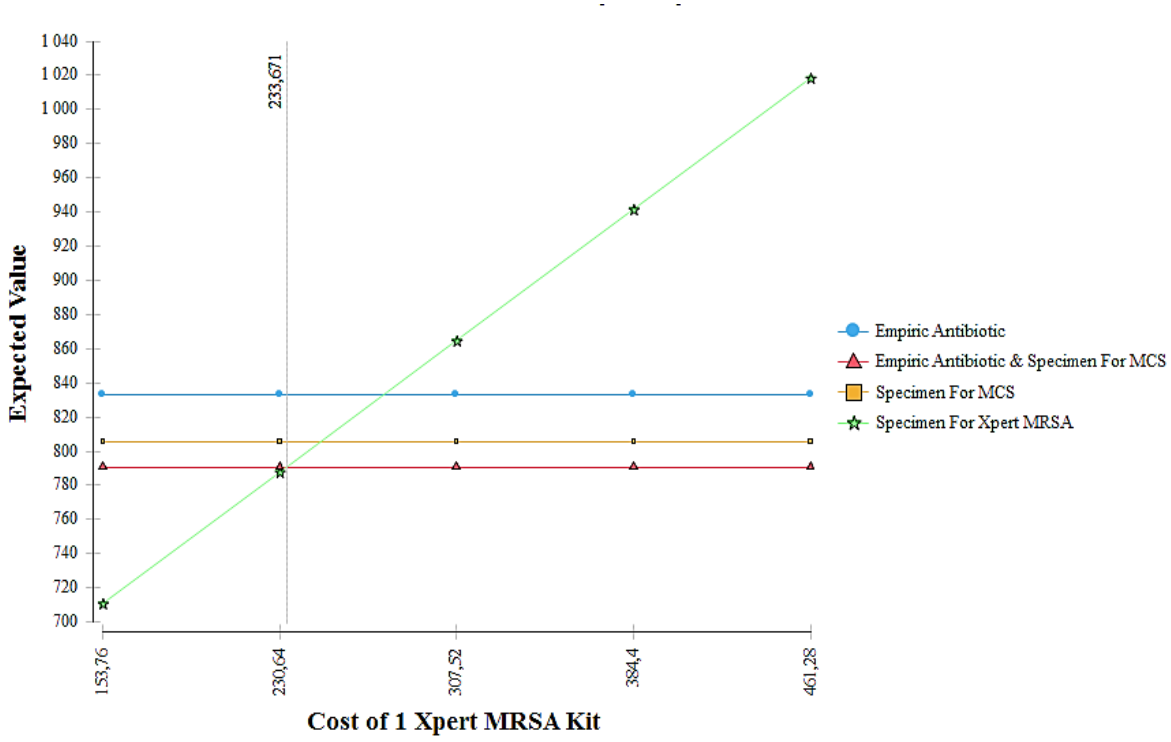


Figure 28: One-Way Sensitivity Analysis Graph for the Variable cXpertMRSA in the Actual Decision-Tree-Analytic Model in the Vascular Ward

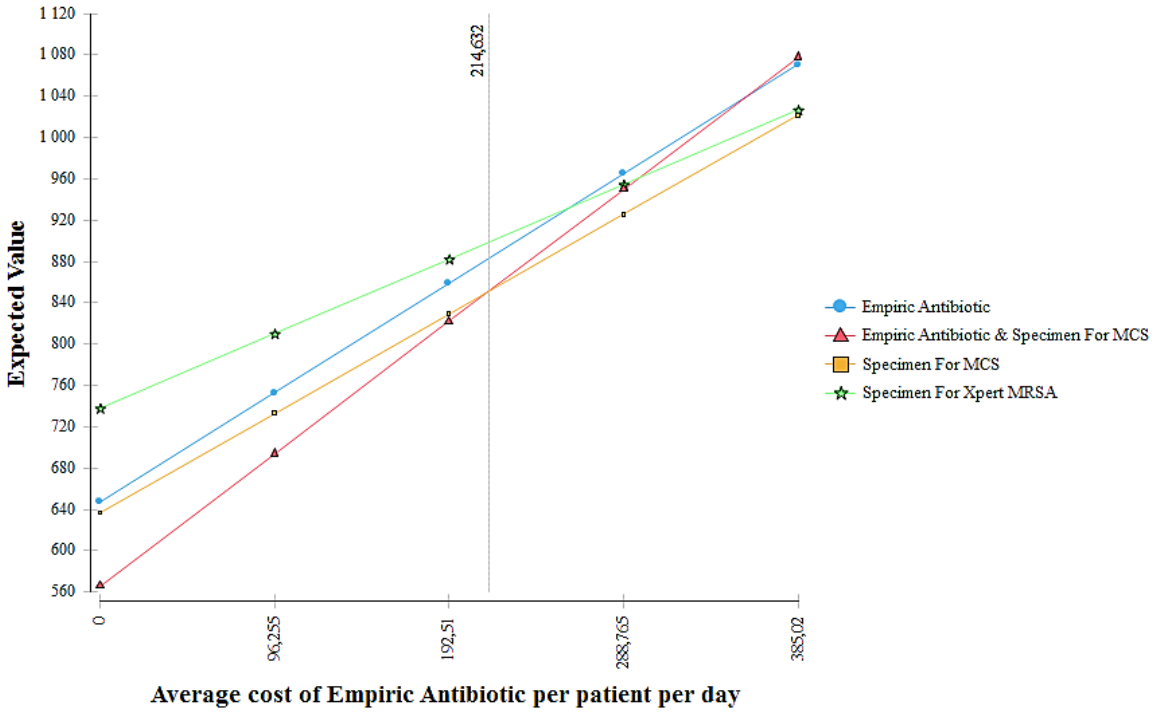


Figure 29: One-Way Sensitivity Analysis Graph for the Variable cDailyEmpiricAntibiotic in the Actual Decision-Tree-Analytic Model in the Vascular Ward

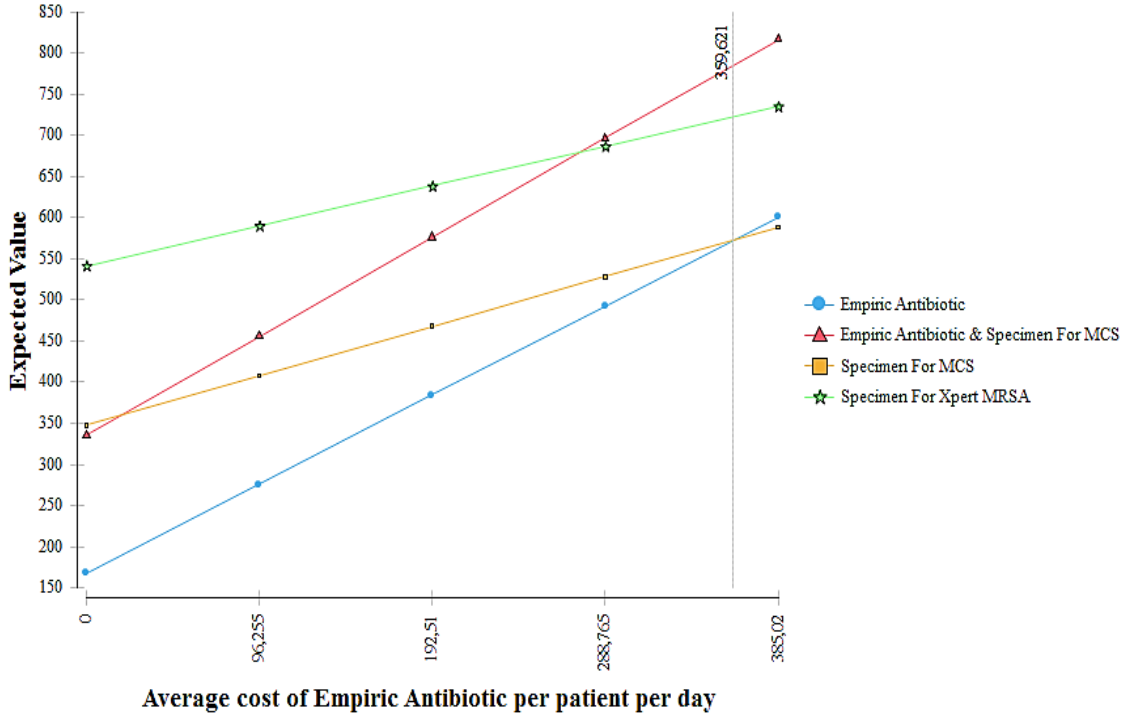


Figure 30: One-Way Sensitivity Analysis Graph for the Variable cDailyEmpiricAntibiotic in the Equal Decision-Tree-Analytic Model in the Vascular Ward

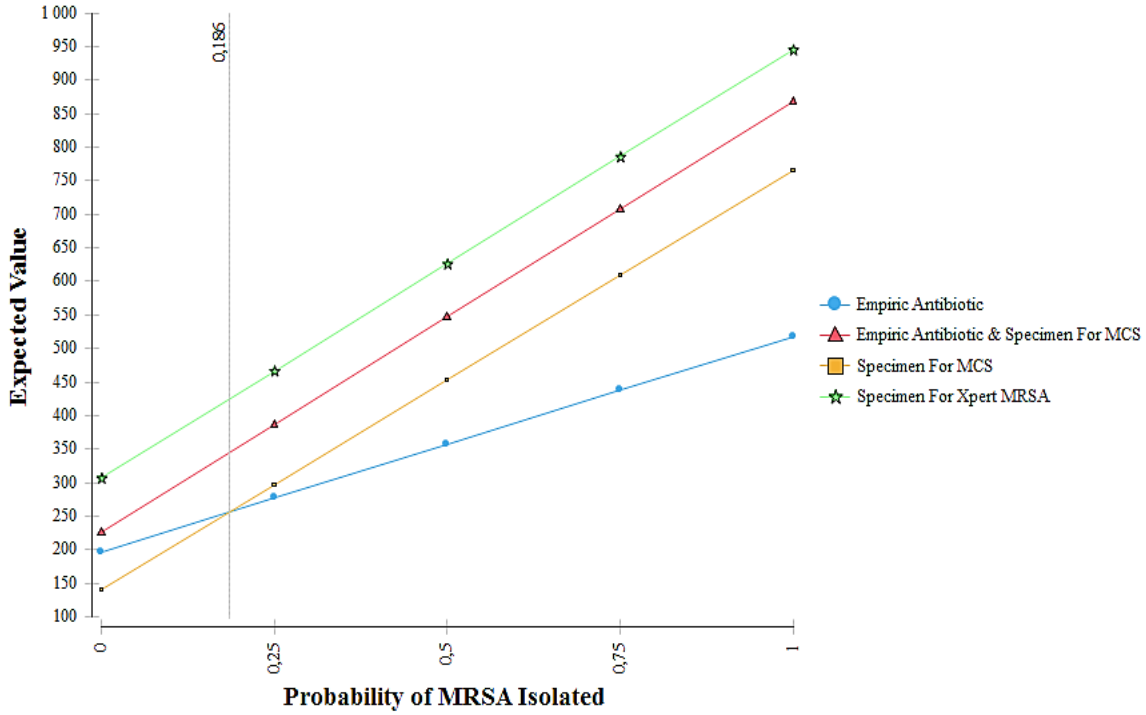


Figure 31: One-Way Sensitivity Analysis Graph for the Variable pMrsaIsolated in the Equal Decision-Tree-Analytic Model in the Vascular Ward

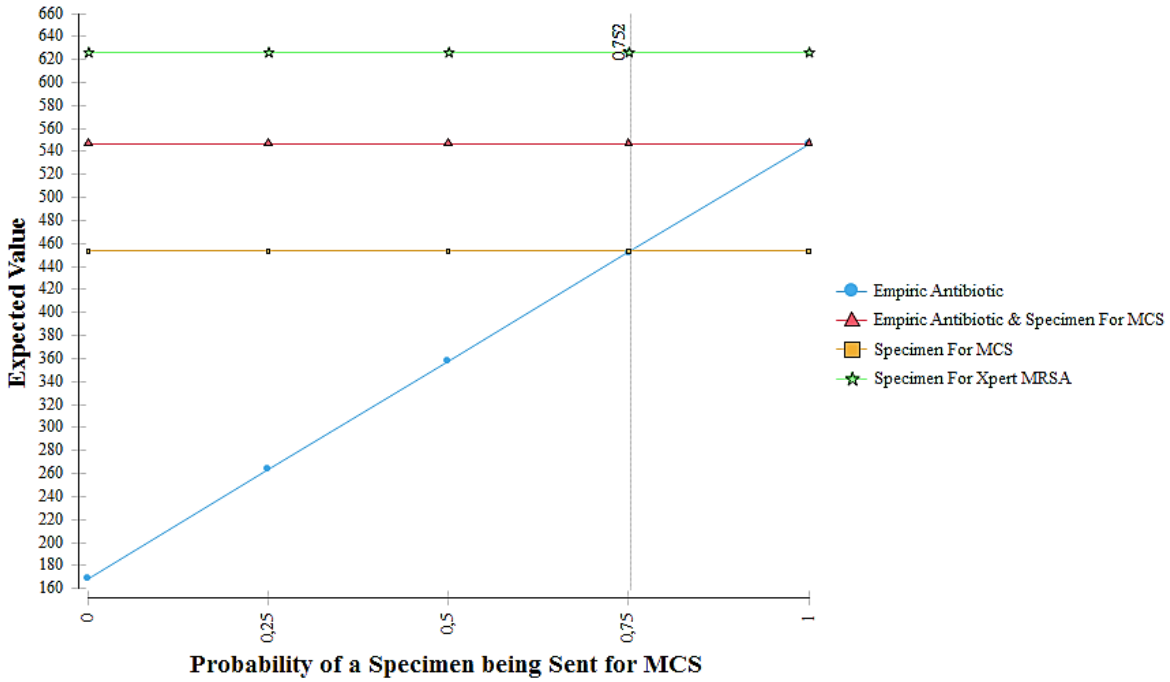


Figure 32: One-Way Sensitivity Analysis Graph for the Variable pSpecimenSentMCS in the Equal Decision-Tree-Analytic Model in the Vascular Ward

For the decision-tree-analytic models with the actual and equal probabilities in the vascular ward, the sensitivity analysis for the variables cSpecimenM, cSpecimenCS, cDailyEmpiricAntibiotic, cXpertMRSA, pConfirmationByCS, pEmpiricAntibiotics, pMrsaIsolated and pSpecimenSentMCS were the same as the sensitivity analysis in the orthopaedic ward, as the same strategies were sensitive and changed as the respective variable changed.

For the variable cDailyOtherAntibiotic, in the actual decision-tree-analytic model, the expected values of the two strategies of Empiric Antibiotics and Specimen For MCS increased as the cost of receiving daily Other Antibiotics increased and in the equal decision-tree-analytic model, the expected value of the three strategies of Empiric Antibiotics, Empiric Antibiotic & Specimen For MCS and Specimen For Xpert MRSA increased as the cost of receiving daily Other Antibiotics increased, thus showing that both models were sensitive to this variable. In the actual decision-tree-analytic model, the expected value of the three strategies of Empiric Antibiotics, Specimen For MCS and Specimen For Xpert increased as the cost of receiving daily MRSA-Specific Antibiotics increased. However, in the equal decision-tree-analytic model, the expected value of the strategy Empiric Antibiotic & Specimen For MCS also increased, in addition to the other three strategies, as the cost of receiving daily MRSA-Specific Antibiotics increased and hence was sensitive to the cDailyMrsaSpecificAntibiotic variable.

Regarding the sensitivity analysis conducted for variables representing the equal probabilities in the vascular ward, the results that were different to the orthopaedic ward are discussed below. For the variable pMrsaSpecificAntibiotics, the expected value of all four strategies increased as the probability of receiving MRSA-Specific Antibiotics increased. The expected value of the three strategies of Empiric Antibiotics, Empiric Antibiotic & Specimen For MCS and Specimen For MCS increased as the variable pOtherAntibiotics increased. A change in expected value indicated that the strategy was sensitive to the variable.

4.5.2.4 Tornado Analysis

Within a Tornado Diagram, each horizontal bar symbolised a one-way sensitivity analysis performed at the decision node for a variable. A thick vertical line in any of the variables' horizontal bar represented a threshold that occurred at the corresponding expected value on the x-axis. Threshold lines that were drawn at the end of a horizontal bar could imply that within a part of the stipulated range, the optimal strategy had an expected value that did not change. The expected value of the optimal strategy was shown on the Tornado Diagram as a dotted vertical line. The thresholds and the expected values represented in these Tornado Diagrams have already been discussed in the previous sections on decision-tree-analytic models. The Tornado Diagrams for the decision-tree-analytic models are shown in Figure 33, Figure **34**, Figure 35 and Figure 36 as well as described below.

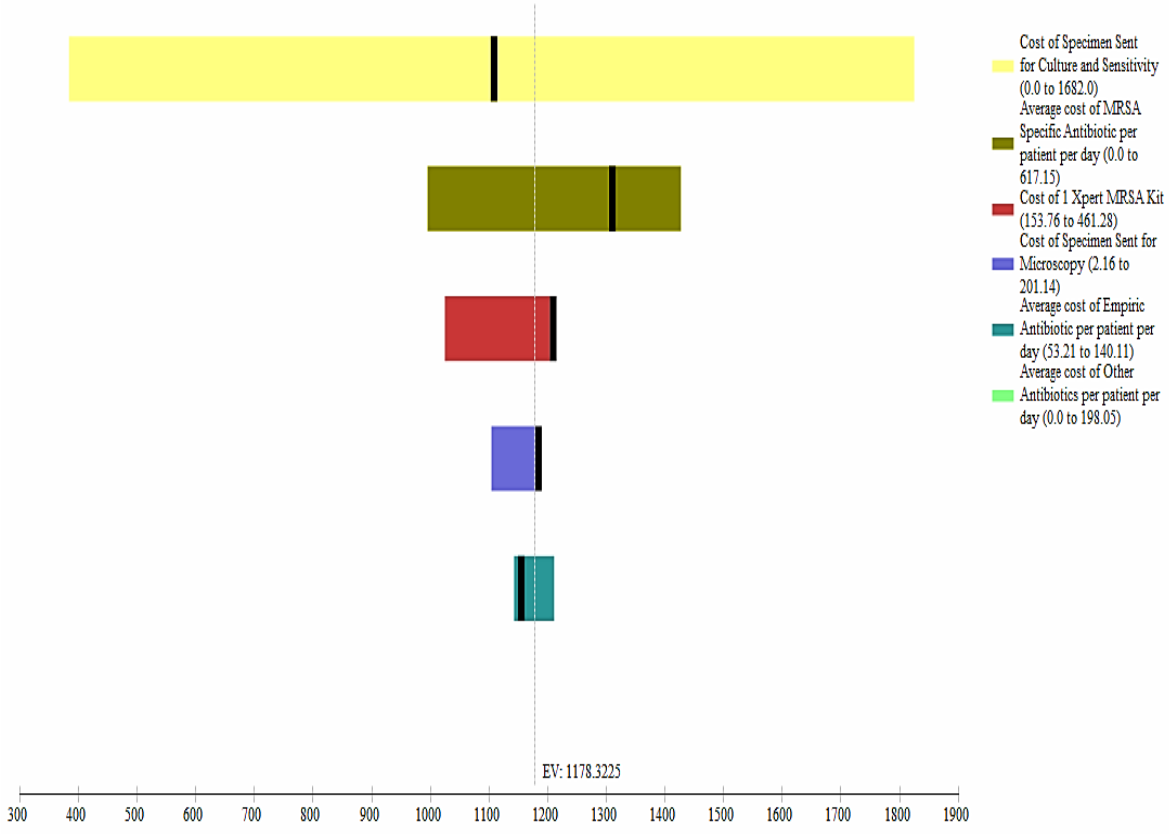


Figure 33: Tornado Diagram for the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward

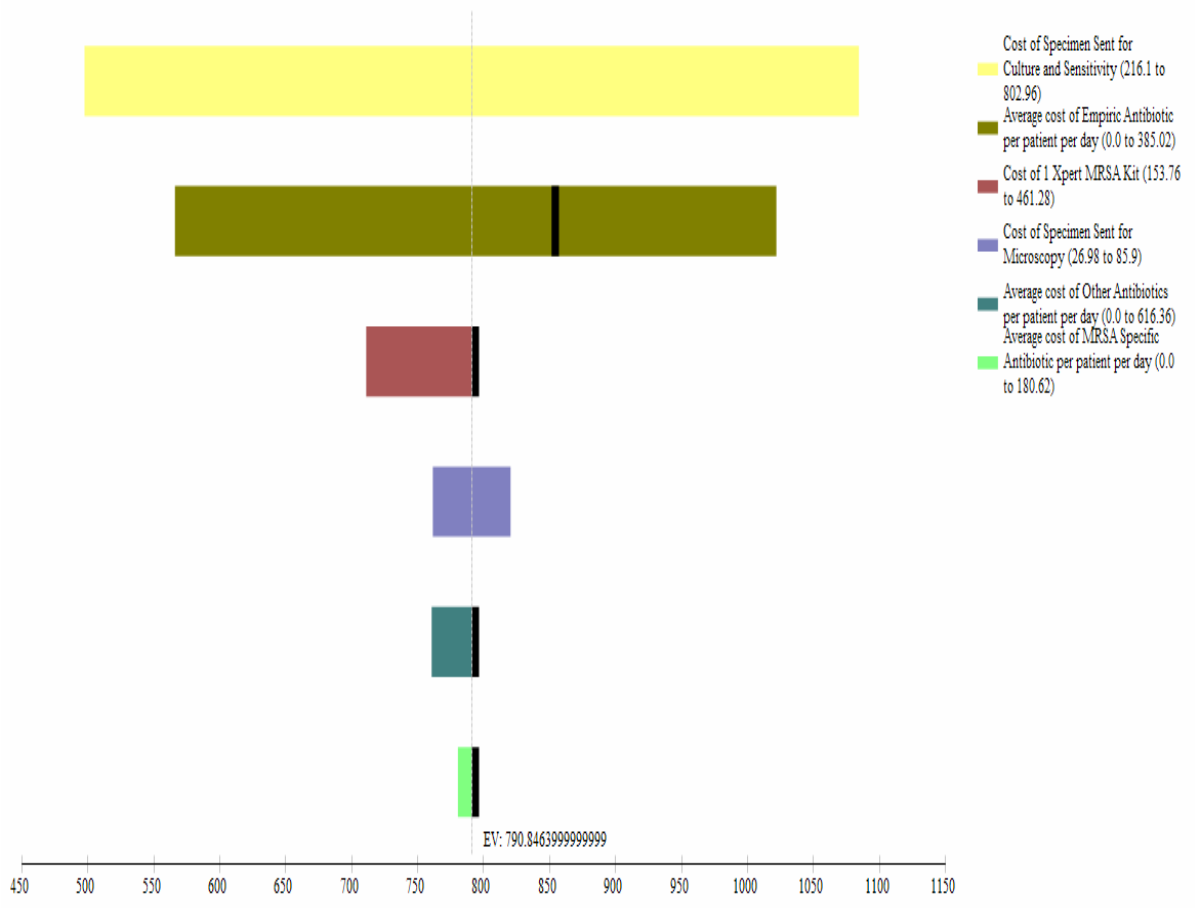


Figure 34: Tornado Diagram for the Actual Decision-Tree-Analytic Model in the Vascular Ward

In the Tornado Diagrams for the actual decision-tree-analytic models in the orthopaedic and vascular wards, the variable cSpecimenCS was displayed as the top widest bar (variable index 0) and thus had the greatest influence on the overall expected value and was the most uncertain variable in the decision-tree-analytic models. In the Tornado Diagram of the actual decision-tree-analytic model in the orthopaedic ward, the variable cDailyMrsaSpecificAntibiotic had a variable index of 1. However, in the Tornado Diagram of the actual decision-tree-analytic model in the vascular ward the variable cDailyMrsaSpecificAntibiotic had the narrowest bar at the bottom (variable index 5) and could be said to have had the least effect on the model's expected value. The variable cXpertMRSA was placed third (variable index 2) in both the tornado diagrams and thus had a moderate effect on the model's expected values.

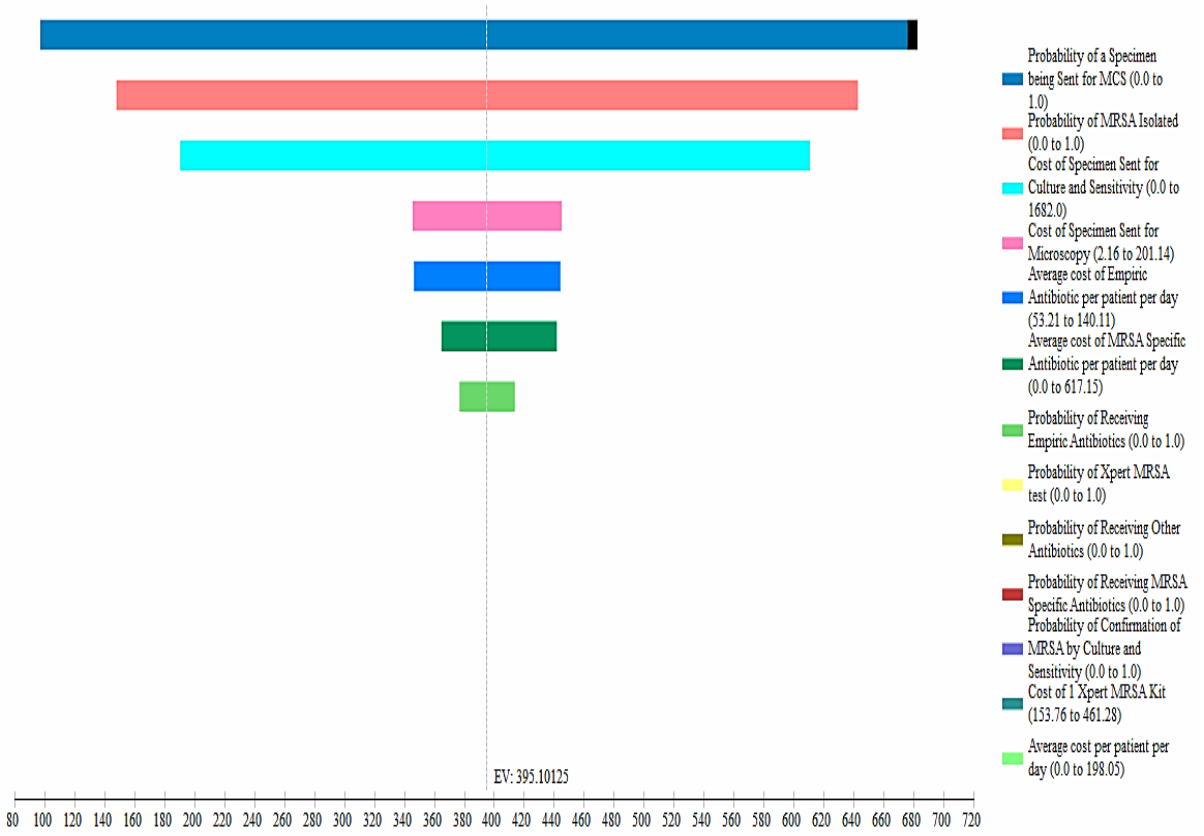


Figure 35: Tornado Diagram for the Equal Decision-Tree-Analytic Model in the Orthopaedic Ward

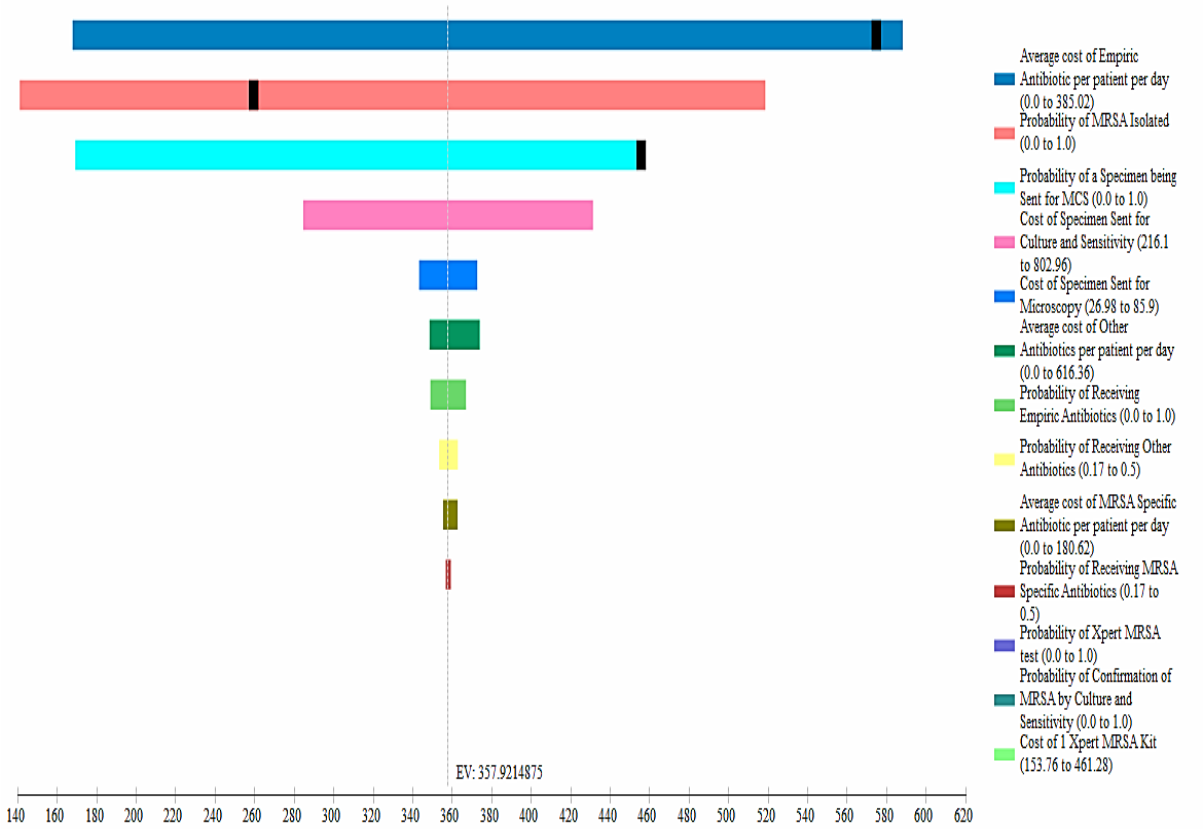


Figure 36: Tornado Diagram for the Equal Decision-Tree-Analytic Model in the Vascular Ward

In the Tornado diagram for the equal decision-tree-analytic model in the orthopaedic ward, the variable pSpecimenSentMCS was displayed as the top widest bar and in the Tornado diagram for the equal decision-tree-analytic model in the vascular ward, the variable cDailyEmpiricAntibiotc was displayed as the top widest bar, thus these variables had the greatest influence on the overall expected value and were the most uncertain variables. The variable cXpertMRSA was the tenth variable (variable index of 10), the third variable from the bottom of the equal decision-tree-analytic models in the orthopaedic and vascular wards, thus suggesting that if equal probabilities were applied to the current clinical settings, the cost of the Xpert MRSA tests would not have a weighty effect on the model's expected values.

5. DISCUSSION

5.1 Overview of Research

PCR test rapidly tests for MRSA within a few hours. Despite the benefits that may be associated with these PCR tests, research needed to be conducted to assess whether it would be cost-effective to implement these tests within the current setting of a South African public hospital. However, once the research began, it was found that there was no baseline data regarding the daily practices, costs and management pathways associated with using the current Conventional Culture Method that is used to test for MRSA in public hospitals in South Africa.

Therefore, the objectives of this study were set. Firstly, to conduct observations in the hospital wards, NHLS Microbiology Laboratory and the main dispensary at CMJAH in order to document the current daily practices relating to MRSA testing and management. Secondly, to carry out a retrospective utilization review of the treatment pathways and laboratory tests conducted, associated with MRSA in the study population. Thirdly, to perform a cost analysis using the utilization and costing data obtained to determine the costs associated with the antibiotics used and the laboratory tests that isolated MRSA in the study population. Lastly, to develop decision-tree-analytic models to compare the current costs and management pathways associated with the Conventional Culture Method versus theoretical situations arising if using the Xpert MRSA tests were to be implemented in the current setting to determine the method that would be most cost-saving in the South African public healthcare setting.

As there are only a limited number of studies in the South African healthcare context which report on the various aspects of this research, international studies were also used as a reference source for discussing and comparing the results obtained in this study. However, a direct comparison could not be made as many factors need to be taken into account when comparing the healthcare setting in South Africa and other countries. The key results from each section of this study are discussed in relation to the current setting as well as the published literature and guidelines.

5.2 Burden of MRSA

In 2014, the WHO published a document entitled *Antimicrobial Resistance: Global Report on Surveillance*, which reflects the global picture of antibiotic resistance in 2013 based on the information that was available. This report acknowledges that although antibiotic resistance is a growing concern globally, there are several gaps of missing information regarding antibiotic resistance due to reasons such as no surveillance or lack of standardised

surveillance methodologies and their implementation in certain areas. As a result, the exact economic extent of antibiotic resistance cannot be measured. The WHO report also highlights that antibiotic resistance is a liability to the economy. However, another alarming gap of missing information is that the true cost of antibiotic resistance is unknown and is largely represented by estimates, thus indicating another area in which information is missing and the need for research to be conducted. In order to efficiently deal with the problem of increasing antibiotic resistance, these gaps need to be filled. These gaps were identified and addressed in the context of this study regarding the current cost and management pathways for a patient with a suspected MRSA infection (World Health Organization, 2014).

Within certain settings, especially amongst high-income countries, surveillance for antimicrobial resistance has already been implemented and is now part of HCPs daily practice. However, within settings such as those in which resources are limited, antimicrobial microbial surveillance has not been implemented and thus there is no consistent surveillance data available for these areas. Thus the WHO collected data from various sources regarding the resistance of antibiotics used in the treatment of infections due to certain bacteria, *Staphylococcus aureus* being one of them. Based on the regions that contributed data relating to MRSA, the percentage of MRSA amongst *Staphylococcus aureus* ranged from 0.3% to 90%. It can be seen in Table 28 that within parts of the region there is a large difference between the smallest and largest value of the overall reported range of resistant proportion. Focusing on the national data obtained from nine countries in the African Region, the overall reported range of MRSA amongst *Staphylococcus aureus* was 12% to 80% (World Health Organization, 2014).

Table 28: The Overall Reported Range of *Staphylococcus aureus* Resistance to Beta-lactam Antibacterial Drugs (MRSA) Obtained from Data Sources in Various Regions (Adapted from: World Health Organization, 2014, Table 7)

Data Sources (minimum of 30 tested isolates) (n = Number of Countries)	**Overall Reported Range of Resistant Proportion (%)**
African Region: National data (n=9)	12 – 80
Region of the Americas: National data or report (n=15)	21 – 90
Eastern Mediterranean Region: National data (n=4)	10 – 53
European Region: National data or report (n=36)	0.3 – 60
South-East Asia Region: National reports (n=3)	10 – 26
Western Pacific Region: National data (n=16)	4.0 – 84

5.2.1 Burden of MRSA in South Africa

The WHO report mentioned above also provided details of the percentage of resistance within individual countries. In South Africa, the prevalence of MRSA amongst *Staphylococcus aureus* infections was 52%. This data was obtained from national data that tested 1 177 invasive isolates samples in 2012 (World Health Organization, 2014).

A systematic review conducted by Nyasulu and co-authors (2012), entitled *Antimicrobial Resistance Surveillance among Nosocomial Pathogens* investigated the prevalence of resistance of antimicrobial drugs in organisms, one of them being *Staphylococcus aureus*. This review included studies from both public and private hospitals in South Africa between 2000 and 2009. Due to different methodologies used in the studies included, resistance to both cloxacillin and methicillin was reported. Therefore, the prevalence of cloxacillin resistance amongst *Staphylococcus aureus* isolates was 29% and the prevalence of methicillin resistance amongst *Staphylococcus aureus* isolates was 33% (Nyasulu *et al.*, 2012).

Studies focusing specifically on the percentage of MRSA in either private or public hospitals in South Africa have been conducted. Within the South African private hospitals included in a study, the percentage of MRSA ranged from 29% to 46% during the period January 2006 to June 2006 (Brink *et al.*, 2007). Comparatively, within the South African public hospitals included in a study, the percentage of MRSA ranged from 24% to 59% during 2010 (Bamford *et al.*, 2011). Although these results are taken from different settings and times and a direct comparison cannot be made, it may be suggested that South African public hospitals had a higher rate of MRSA than South African private hospitals.

A further report, *Antimicrobial Resistance Surveillance from Sentinel Public Hospitals, South Africa, 2013,* obtained data on antimicrobial susceptibility testing regarding common organisms isolated from blood cultures at various public hospitals in South Africa during a 12-month period. 2 424 *Staphylococcus aureus* isolates from blood cultures were recorded at the selected public hospitals in 2013. The number of cases of *Staphylococcus aureus* isolates from blood cultures ranged from 186 to 227 per month. Of the *Staphylococcus aureus* isolates that were tested with cefoxitin, 41% were reported to be resistant to cefoxitin and thus considered to be MRSA. However, only 37% of the *Staphylococcus aureus* isolates that were tested with oxacillin and other beta-lactam antibiotics were recorded as resistant. Focusing specifically on CMJAH, 41% of the *Staphylococcus aureus* isolates that were tested with Cefoxitin were resistant, as compared to 47%, 40% and 18% recorded respectively at Chris Hani Baragwaneth Hospital, King Edward VIII Hospital and Nelson Mandela Academic Hospital respectively (Perovic *et al.*, 2014).

Another study focusing on cases of *Staphylococcus aureus* bacteraemia in three academic hospitals in South Africa, between September 2012 and September 2013, reported that overall MRSA was present in 36% of these cases. The individual percentages of MRSA isolates amongst the cases of *Staphylococcus aureus* bacteraemia per hospital were reported as 24% in Helen Joseph Hospital, 26% in Steve Biko Academic Hospital and Tshwane District Hospitals and 58% in CMJAH which had the highest percentage (Fortuin-de Smidt *et al.*, 2015).

As a variance in the percentage of MRSA resistance amongst *Staphylococcus aureus* isolates in South Africa can be seen from the studies above, it is important to consider the factors that could account for this variance such as the hospitals that were included in the report and the types of samples that were used to obtain data regarding the isolates

5.3 Study Population

The data received from the NHLS Corporate Data Warehouse Information Systems was used to derive the study population. After sorting and filtering the data as well as setting the inclusion and exclusion criteria, the orthopaedic ward and vascular ward were included in the study population. The literature below also demonstrates that patients in the orthopaedic and vascular wards are amongst the patients that are more susceptible to infection with MRSA.

There are various factors that predispose patients in the orthopaedic ward and undergoing orthopaedic surgery to infections due to MRSA. These factors include but are not limited to undergoing surgery, insertion of invasive medical devices, having prostheses or supporting structures and immobilisation after operations (Lee *et al.*, 2010). These factors can also be identified in the patients in this study population that had MRSA in the orthopaedic ward, as they underwent surgery and post-surgical procedures as well as having supporting structures such as prosthesis, nails or plates.

As noted by Lee and co-authors (2010), there are several similarities between patients in an orthopaedic ward and patients in a vascular ward, such as having co-morbidities, being elderly and in most cases undergoing planned elective procedures more often than unplanned emergency procedures. However, there are also noticeable differences between these two groups of patients (Lee *et al.*, 2010). These differences can be recognised in the patients in this study population as although the patients in both wards had underlying conditions and underwent surgical procedures, the types of conditions and procedures differed between the two wards.

The nature of both orthopaedic surgery and vascular surgery is invasive. However, in orthopaedic surgery the bacterial contamination remains more localised due to the procedures involving articular spaces and soft tissue as compared to vascular surgery, in which bacterial contamination can easily move and spread as the procedures involve creating a direct opening into the bloodstream, as well as the possible occurrence of vascular insufficiency (Lee *et al.*, 2010).

Patients in the vascular ward diagnosed with vascular disease often also have conditions such as poor circulation, diabetes, chronic sepsis, ulcers and gangrene, which make them vulnerable to acquiring infections due to MRSA. It has been shown that in certain countries MRSA is a main cause of infection in patients that had vascular surgery as well as infections in vascular wounds and grafts (Earnshaw, 2002). These conditions were also identified in the patients in this study population that had MRSA in the vascular ward, as many of them had diabetes, hypertension, PVD and a form of sepsis. Not only has infection due to MRSA become common amongst patients undergoing vascular surgery, it has additional critical consequences such as increased need for amputation and removal of grafts (Lee *et al.*, 2009).

In both of the wards, there was a wide range regarding length of stay in hospital. The orthopaedic ward had an average of 48 days in hospital and the vascular ward had an average of 38 days in hospital. Studies have found that a patient with an infection due to MRSA would have a longer stay in the orthopaedic and vascular wards compared to those patients without an MRSA infection; however, the number of additional days varies between the studies. A study conducted on vascular surgery patients reported the median number of days that a patient with MRSA stayed in hospital was 24 days (Cowie *et al.*, 2005) and a study conducted on orthopaedic surgery patients reported the average number of days that a patient with MRSA stayed in hospital was 88 days (Tai *et al.*, 2004). The variation in the number of days spent in hospital for patients with HAIs may also be due to factors such as their age, initial diagnosis, co-morbidities, surgical procedures and overall well-being. An additional factor is that while patients with HAIs experience a prolonged stay in hospital, they are at a high risk of acquiring HAIs (Schulgen *et al.*, 2000).

5.3.1 Patient Characteristics and Demographic Data

Although the objective was to perform a utilization review of the antibiotics administered and laboratory tests conducted with the results of MRSA in order to formulate management pathways for patients in the study population, basic demographic data was first collected to gain an understanding of the study population. The factors that could predispose patients in

an orthopaedic or vascular ward to acquire an MRSA infection have been discussed. However, in light of the study's results, the following can be emphasised.

The median age of the patients in the orthopaedic ward (45 years) and vascular ward (59 years) was much younger than the median ages that are common in patients undergoing orthopaedic surgery (65 years) (Lee *et al.*, 2010) and vascular surgery (73 years) (Lee *et al.*, 2009). In both wards, more than half of the patients were male, which correlates to a study which found that males are at a higher risk for MRSA than females, despite previous research which demonstrated no noticeable difference of the risk of MRSA in males and females (Kupfer *et al.*, 2010)

5.4 Ethnographic Observations

Qualitative research methods of ethnography and inductive analysis were used to collect, record and analyse the data obtained from the observations (McMillan *et al.*, 2014). The observations conducted in the CMJAH orthopaedic and vascular wards as well as the NHLS Microbiology Laboratory and Main Dispensary, aided in gaining an understanding of the current clinical practices of HCPs when managing a patient with a suspected MRSA infection, the current method used to test for MRSA in the laboratory and the current process of dispensing antibiotics to inpatients. Having this understanding also assisted this study when interpreting the retrospective patient records, formulating the patient management pathways, performing the cost analysis and developing the decision-tree-analytic models.

5.4.1 Clinical Ward Observations

The clinical ward observations were conducted only during the morning ward rounds over a period of one week per ward, therefore the information discussed below is based only on the practices observed and cannot be taken as a general comment on the wards. Another point is that only the general practices were observed qualitatively and a quantitative assessment was not conducted thus, it is not possible to make direct comparison to many studies that quantitatively report on the various aspects in the ward, infection control and treatment of patients with MRSA.

Although similar practices were noticed in the orthopaedic ward and the vascular ward regarding HCPs practices during the morning ward rounds, the similarity in the practices was not always due to similar protocols being followed in these two wards, nor could it imply that they were the ideal practices. A pattern identified was that within the wards, certain practices of the HCPs were done routinely, while others were inconsistent.

5.4.1.1 Ward Rounds

Routinely, every morning, an HCP and a nurse would start the ward round in order to follow the progress of each patient, and during the course of the ward rounds, other HCPs would join or leave the team. As observed in the ward rounds in this study, ward rounds have been described by other studies as a time during which various HCPs meet to discuss patients' management pathways (Liu *et al.*, 2013). It is also common practice in other hospitals to have a multi-disciplinary team present during ward rounds, as observed in CMJAH, although the actual members present may differ between hospitals (Busby *et al.*, 1992)

It was observed that during a patient's stay in the ward, different HCPs with the same qualifications would attend to the patient. Being treated by numerous HCPs may impose possible disadvantages to the patient such as:

- It is time-intensive to establish which tests were requested by the previous HCPs and then to follow up if these tests were actually conducted and if the results were received and interpreted.
- If the laboratory test information is not easily accessible, the same tests may be reordered and conducted, resulting in unnecessary costs and use of resources.
- Repeat medication prescriptions were made even though they were already prescribed on the current prescription chart.
- Medicines were not signed off to discontinue the medication before prescribing an alternative.
- Differing styles of the HCPs patient notes in the patient's record, thus making it difficult to look back and understand the patient's complete history without suspecting that information was missing. For example: detailed notes compared to basic points.

Observing these patterns helped in understanding certain aspects when extracting data from patients' retrospective records.

During the ethnographic observations, the different forms of communication were observed and included in the pattern of Underlying Themes. Despite there being numerous HCPs on the team and in the wards, the communication observed between the HCPs present was good, as there was a level of understanding and respect. However, the communication observed between some of the HCPs and the patients seemed to be lacking and brief. Absence of communication between HCPs and patients is neither a unique nor new issue during ward rounds, as studies dating back to the 1960s discuss the implications and the importance of improving this issue (Busby *et al.*, 1992; Ha *et al.*, 2010).

5.4.1.2 Infection Control Practices

When applying for ethics, hospital and ward approval to conduct this study, it was stated that the infection control practices of the HCPs would be observed and thus permission was granted to do so. However, in order to obtain a clear reflection of what happens in daily practice in the wards, only once the observations in the wards were complete was an enquiry made as to whether there are formal documented protocols in place regarding infection control in the wards. The Infection and Prevention Control Protocols (27/08/2013) that were made available in the ward were very general and thus a comparison to the observations could not be made. After much further enquiry, it could not be established whether or not there were other documented protocols that had not been made available, or if the HCPs currently in the ward were themselves unaware of additional protocols, or if those were actually the only documented protocols regarding infection control in the wards.

A pattern of inconsistency was identified when analysing the infection control practices that were observed in the wards. During the observed ward rounds, antiseptic/disinfectant hand-rub and hand washing basins was easily accessible and available in the wards; however, they were not always used as required. These practices varied between the different HCPs that were present on the ward rounds. Inconsistent hand washing practices are not uncommon. Globally there are numerous guidelines and studies relating to hand washing practices in the healthcare environment. In 2009, the WHO published the *WHO Guidelines on Hand Hygiene in Health Care,* which was formulated by a panel of specialists and implemented in healthcare settings of various economic rankings worldwide, thus emphasising the global nature and importance of correct hand washing practices (World Health Organization, 2009).

This guideline consists of consensus recommendations for hand hygiene such as: Indications for hand hygiene; Hand hygiene techniques with Alcohol-Based Formulation or Soap and Water; Recommendations for surgical hand preparation; donning and removing non-sterile and sterile gloves. It also includes the model “The five moments for hand hygiene in health care” which are:

1. Before touching a patient
2. Before a clean/aseptic procedure
3. After body fluid exposure risk
4. After touching a patient
5. After touching patient surroundings

This model is incorporated in the WHO Multimodal Hand Hygiene Improvement Strategy and has already been implemented in numerous hospitals (World Health Organization, 2009).

It is well established that correct hand washing practices can prevent the further spread of infections. A recent review was conducted by looking at other studies to determine the extent to which hand hygiene practices affect the transmission of MRSA. The review concluded that the spread of MRSA is reduced by correct hand hygiene practice, however, studies need to be conducted to determine the exact extent and also the effects of other factors such as contact precautions (Marimuthu *et al.*, 2014).

Regarding the isolation practices for patients identified with MRSA, the pattern of lack of resources in terms of hospital space was recognised. The HCPs identified the need to isolate patients displaying signs of serious infection, but due to the lack of resources at times there were no specialised isolation areas within the two wards in order to implement the correct isolation procedures. The HCPs therefore had to take alternative courses of action, which even included moving the patient with an infection to the far corner of the current ward. As with most infection control practices, different hospitals implement different strategies depending on their available resources. As MRSA easily spreads, isolation may play an important role in the prevention of further MRSA infections. However, there is much controversy regarding the effectiveness of isolation practices, as there are certain disadvantages to isolating patients. In addition to the extra resources and costs associated with isolating a patient (Gould, 2006), the psychological effects of isolation on the patient and the HCPs work attitude towards isolated patients also have to be taken into account (Halcomb *et al.*, 2008; Fätkenheuer *et al.*, 2014; Seibert *et al.*, 2014).

5.4.1.3 Treatment of Patients

The HCPs actions taken for a patient presenting with a suspected or confirmed infection were observed during the morning ward rounds. The nurses were consistent in routinely measuring the patients' temperatures, as an increased temperature may indicate the presence of a suspected bacterial infection (Gopalan, 2005; Boyles *et al.*, 2015). A pattern of routine was identified when analysing the steps taken for a patient with a suspected infection as the HCPs would always instruct that a septic work-up be performed and would stipulate which tests were to be done and if there was a need for empiric antibiotics to be administered while waiting for the test results. Although it is common practice for HCPs to initiate a septic work-up for a patient with suspected infection, a study conducted by O'Grady and co-authors (2008), concluded that when a patient presents with an increase in temperature, HCPs should not routinely order laboratory and other tests to be conducted, but should rather first perform a thorough clinical examination on the patient due to the fact that presence of fever does not necessarily mean the presence of infection. In this way unnecessary laboratory tests costs can be avoided.

A South African article acknowledges that in certain cases it can be challenging to diagnose HAIs. Despite there being various guidelines available to aid the diagnosis of infection and sepsis, presentation varies and some of the features mentioned to assist in the diagnosis of infection or sepsis are common features that most hospitalised patients present with, irrespective of whether they have an infection or not. Therefore, it is important that the patient's medical records are used along with a clinical assessment to guide the diagnosis of an infection. In order for HCPs not to miss the presence of infection in a patient the HCPs should also be aware that certain groups of patients may not present with the common features of infection. HCPs also need to be aware that systemic features of infection may not be present in a patient with a localised infection (Gopalan, 2005).

However, once the initial identification of a suspected infection and the ordering of a septic work-up were performed, patterns of disorganization, lack of communication, waiting and unavailable resources were identified. These included:

- Looking for information by paging through the patient's records or piles of paper at the front of the ward.
- Re-ordering of laboratory tests if the patient's MCS test results were not easily located.
- Continuing with Empiric Antibiotics following confirmation of MRSA whilst waiting for motivation for MRSA-Specific Antibiotics from senior HCPs.
- Continuing with Empiric Antibiotics following confirmation of MRSA if the patient's clinical signs were not deteriorating.

5.4.2 NHLS Microbiology Laboratory Observations

To gain an understanding of the current process of identifying MRSA, ethnographic observations were conducted at the Bacteriology bench of the NHLS Microbiology Laboratory at CMJAH. When a specimen for a suspected infection was received at the laboratory, the Conventional Culture Method was used to identify the type of infection. The Conventional Culture Method consists of three main steps: Microscopy, Culture and Sensitivity, as well as two preparation steps of Planting and Picking.

The Conventional Culture Method has been considered as the traditional method for the detection of MRSA (Havill, 2010). However, due to the limitations of this method such as its resource-intensive and time-intensive nature, researchers have continually been trying to develop an optimal method of detection for MRSA, hence the wide variety of MRSA testing techniques currently available. The Conventional Culture Method for the detection of MRSA consists of different phenotypic tests such as agar screening, disc diffusion, minimum inhibitory concentration and E-tests. The newer methods for the detection of MRSA use

genotypic techniques using PCR. Studies have been conducted to try and detect which method or combinations of methods are best at detecting MRSA (Adaleti *et al.*, 2008; Datta *et al.*, 2011).

Upon analysing the data collected for the process of conducting the Conventional Culture Method, various patterns were deduced. The overall patterns that were identified when following the steps taken from when a specimen was received until a diagnosis was made were ones of routine, organization and systems. There were established routines and documented protocols in place that were followed systematically by the laboratory personnel during each step of conducting the Conventional Culture Method. The equipment and resources that were required to perform each step were well organised and easily accessible within the laboratory. However, in a healthcare setting in which resources are scarce, it was found that the Convention Culture Method is resource-intensive.

Although there were a number of laboratory personnel that worked at the bacteriology bench, they worked well together as a team and would often ask each other for opinions when reading the plates. The Conventional Culture Method as such, largely relies on the laboratory personnel's skill and expertise in preparing the plates, as well as their knowledge and judgement when reading the plates to identify possible organisms. This method also requires various techniques and tests to be conducted in order to obtain the diagnosis and the details of the organism identified. Therefore, different laboratory personnel perform different steps of the Conventional Culture Method and in this manner it serves as a double checking process to ensure that the previous step was prepared and had been read appropriately to ensure the accuracy of the results. At the end of the Conventional Culture process, before a patient's results are finalised, they are first checked by a pathologist. Thus as observed, as well as documented, the Conventional Culture Method is not only a time and resource-intensive process, but also a labour-intensive process (Huletsky *et al.*, 2005).

Another pattern observed was the time involved in the Conventional Culture Method. Firstly, the nature of this method requires plates to be incubated for certain periods of time before they can be read, thus accounting for a three to five day wait before the confirmed test results are available. Secondly, the actual preparing and reading of the plates by the laboratory personnel is a time-intensive, tedious and hands-on task. The new PCR methods for the detection of MRSA are less time-intensive and provide the test results within a shorter period as compared to the traditional culture methods for the detection of MRSA; however, these new PCR tests are more costly (Havill, 2010).

Thirdly, it was observed that once the laboratory personnel had read each plate, they would write down the results on the corresponding patient's working card. On completion of reading all the plates, these results would then be entered onto the computer system and would be accessible to the HCPs as provisional results. However, this current system entails a time-intensive double entering of results. If the results were entered straight onto the computer system, not only would this time be saved, but the HCPs would have the results sooner.

The observations provided the knowledge in order to understand the costing system used for patients that had MCS tests done, as well as gave perspective on the timing and waiting periods that occur in the wards.

5.4.3 Antibiotic Dispensary Observations

To obtain a complete understanding of the management of patients with a suspected or confirmed infection, ethnographic observations were conducted in the antibiotics designated area of the dispensary at CMJAH. When interpreting the results regarding the procedure for dispensing antibiotics to inpatients, the patterns that were revealed alternated between routine and flexibility.

Although there were no formal printed protocols available, the current antibiotic dispensing procedure that was executed was explained. As there was an established dispensing process that took place between the wards and dispensary, a pattern of routine was identified. Simultaneously, a pattern of flexibility was also present, as the dispensing process could differ slightly per patient depending on the severity of each patient's condition. It was also said that although each ward had a dispensing system with the dispensary, the system kept on changing and could differ between wards as well as between different hospitals. Thus the pattern of flexibility appeared again.

Along with the advancement in information and communication technology, there have been numerous developments in the area of hospital dispensing systems such as Automated Dispensing Cabinets (Rodriguez-Gonzalez *et al.*, 2012), and Electronic Medical Records. However, in both developed and developing countries, research is being conducted regarding the implementation and benefits of these new systems (Fraser *et al.*, 2005; Blaya *et al.*, 2010). The dispensing system currently used between the wards and the dispensary is a manual one that involved the doctor writing prescriptions on the patients' prescription charts; the nurse copying the prescriptions onto dispensary order forms; runners taking the forms to the dispensary; the pharmacist selecting and preparing the required antibiotics to be dispensed; and runners later returning to the ward with the antibiotics.

Once the antibiotics were in the ward it was then the responsibility of the nurses to administer and manage the ward stock. Although not always according to protocol, the nurses had their own system by which they managed the ward stock. As most antibiotics were dispensed on a per patient basis, if a patient no longer required an antibiotic that had been dispensed to the ward for that patient, then the nurse would often use that antibiotic for another patient requiring that same antibiotic, who was in the process of waiting for their prescription to be dispensed. When obtaining data from the patients' retrospective records, this information helped in understanding the differences in waiting periods for antibiotics. Thus, patterns of responsibility, routine and flexibility were evident regarding the management of ward stock by the nurses. An article by Schellack and Meyer (2010), acknowledges that nurses perform most of the duties pertaining to the management of pharmaceutical ward stock, thus providing guidelines for the nurses pertaining to ward stock management. Certain aspects of these guidelines were similar to the observations in this study and the authors also emphasise the importance of continuous communication between the nurses in the wards and the pharmacist (Schellack *et al.*, 2010).

Patterns of restriction and requirements also emerged in the dispensing of certain antibiotics as an attempt to prevent further antibiotic resistance. Within the main dispensary of CMJAH, there was a small designated room for the storage and dispensing of antibiotics which had strict access rules in order to control the flow of antibiotics within the hospital. Stipulated documents such as motivations signed by senior HCPs and microbiology laboratory results were required per patient per antibiotic, in order to authorise the dispensing of specific antibiotics. Although these measures were designed to ensure the use of only essential antibiotics, the waiting for HCPs to sign motivations, or for the laboratory to release the patient's results, could cause delays for patients urgently requiring treatment. The dispensary is therefore flexible in urgent cases.

In 2014 The Centers for Disease Control and Prevention documented the *Core Elements of Hospital Antibiotic Stewardship Programs*, and recommended that Antibiotic Stewardship Programmes should be implemented in all acute care hospitals. It also acknowledges that one universal Antibiotic Stewardship Programme is not possible as it would depend on individual hospitals, but that there are core elements that should be included in these programmes. One of the core elements is to "Implement Policies and Interventions to Improve Antibiotic Use", which consists of broad interventions such as prior authorisation, which was seen in this study. Another broad intervention which, if implemented in this current study could prove to be beneficial is Antibiotic 'Time-outs', which requires that antibiotics prescribed to patients are reassessed after 48 hours by HCPs answering key questions (Centers for Disease Control and Prevention, 2014).

The presence of antibiotic stewardship was observed within the wards and in the antibiotics designated area of the dispensary. Patterns of establishment, improvement, strengthening and necessity were identified. It was deduced that currently, pharmacists are not actively involved in the antibiotic stewardship programme and that it was vital that the current antibiotic stewardship programme be strengthened by actively including pharmacists. Another Core Element of the *Core Elements of Hospital Antibiotic Stewardship Programs* is "Accountability and Drug Expertise", which includes having one leader in charge of the overall antibiotic stewardship programme and one pharmacy leader as well as key support from other HCPs such as clinicians, nurses and laboratory personnel (Centers for Disease Control and Prevention, 2014). A review article by Mendelson (2015), suggests ways in which antibiotic stewardship could be implemented at a patient and programme level in order to assist in preventing the increasing problem of antibiotic resistance.

The pharmacist in this study felt there would be numerous benefits if a strong antibiotic stewardship programme were to be established in the hospital. Amongst other things, an antibiotic stewardship programme would improve the relationship between the prescribers, nurses and the pharmacist; decrease the waiting period between prescribing and administration; facilitate implementation of standardised protocols; ensure optimal utilization of available resources including antibiotics; and ultimately prevent the emergence of antibiotic resistance. In South Africa, key antibiotic stewardship organizations included the Global Antibiotic Resistance Partnership–South Africa and the SAASP. The Department of Health has now developed and implemented the Antimicrobial Resistance National Strategy framework 2014-2024 with the purpose of improving patient outcomes, preventing antibiotic resistance and providing a framework for managing antibiotic resistance (Department of Health, 2014).

5.5 Retrospective Records Review

As established from observations in the wards, patient records are kept manually by HCPs writing in the patient's record. Once a patient is discharged, and after a period of time, the patient records are sent to the Hospital Medical Records Room to be stored. Within the Records Room the patient's record is transferred onto microfiche cards and then stored in drawers according to the patient's hospital number. Due to the limitations of manual paper patient records and with technological advances, hospitals globally are now implementing the use of electronic patient records. However, in the study areas at CMJAH this has not yet been introduced. The limitations arising from using the manual paper patient records system as seen in this study and documented from other studies, include patient records that were missing; duplication of information; disorganization of records; inconsistency between the quality and quantity of notes written by different HCPs (De Wet *et al.*, 2001). The electronic

patient records system seems to address these limitations, as well as has the further advantages of being able to identify, prevent and reduce medication errors (Radley *et al.*, 2013), and assist in antibiotic stewardship (Dalton *et al.*, 2015). However, there are also possible disadvantages in using electronic patient records such additional costs and training required (De Wet *et al.*, 2001). Therefore the feasibility of implementing the electronic patient records system in the context of each hospital should first be assessed.

The retrospective records of the patients in this study population were accessed and viewed under a microfiche reader. Although ethics and hospital permission were granted for this study as well as approval from the head of the records room to collect the required data was obtained, printing of the records, taking pictures or the use of any electronics was not allowed. Thus the information required was written onto case report forms. Even in the case of newer records that are being scanned as PDF documents and viewed on a computer, the information gained could only be written down. This was a tedious and time-intensive process and extra care had to be taken to ensure that all the required information was correctly written down. An advantage of electronic patient records can be highlighted here, as they can provide researchers with easy access to clinical data (Fraser *et al.*, 2005).

Another advantage of electronic patient records over manual paper medical records is that the paper records are not always filled in completely; at times they are not easily understood by other HCPs; and they can also be misplaced, thus resulting in missing information (De Wet *et al.*, 2001). From the derived study population of patients with MRSA in the orthopaedic and vascular wards, 16.67% of the patient records could not be found in the hospital's records room, or could not be included due to various other reasons such as patient records that were unable to be obtained or missing data within the patient records.

5.5.1 Antibiotic Utilization Review

Information regarding a patient's antibiotic history could be found on the doctors' prescription charts and the nurses' administration charts. The nurses' administration charts were found to be a more reliable source of information, as their administration tables were more completely filled in as compared to the doctors' prescription tables. Where possible, reasonable assumptions could be made, however, due to missing and incomplete prescription and administration charts, 24.27% of the antibiotic prescriptions from the orthopaedic ward and 27.81% of the antibiotic prescriptions from the vascular ward had to be excluded from the analysis. Once again, the consequences of the current manual paper records system being used could be eliminated if an electronic patient record system were to be implemented (De Wet *et al.*, 2001).

The antibiotics prescribed and administered to the patients in this study population were divided into Empiric, MRSA-Specific and Other Antibiotics. The average number of antibiotics that a patient received was five in the orthopaedic ward and four in the vascular ward however, the number ranged from one to 13 in the vascular ward. Interestingly, a majority of the antibiotics administered in both the wards (56.41% in the orthopaedic ward and 43.12% in the vascular ward) were Empiric Antibiotics. A study conducted in ICUs at public and private hospitals in South Africa documented the antibiotic prescriptions of 248 patients. From the patients that were prescribed antibiotics, 73.5% of the patients received Empiric Antibiotics, the average number of antibiotics administered was three and the range of antibiotics prescribed at the same time was from one to ten per patient. Paruk and co-authors (2012) state that the main reason for the high number of concurrent antibiotics was due to new antibiotics being started without the previous ones being stopped, this was also apparent when reviewing the patients' retrospective records in this study.

The percentage of empiric antibiotics could be decreased by decreasing the waiting period for laboratory test results by using rapid tests and improving the current system of communication and organization between the laboratory, the wards and HCPs (Geiger *et al.*, 2013). The use of empiric antibiotics is controversial as it may be considered as unnecessary administration of antibiotics and thus lead to further antibiotic resistance, however, their correct use may be beneficial (Solomkin *et al.*, 2004; Paul *et al.*, 2010).

As all the patients in this study population had a confirmed laboratory diagnosis of MRSA, surprisingly, only 19.27% and 34.62% of the antibiotics administered were MRSA-Specific Antibiotics in the vascular and orthopaedic wards respectively. In both wards, not all of the patients in this study population received MRSA-Specific Antibiotics, as only nine out of the 16 patients in the orthopaedic ward and 11 out of the 29 patients in the vascular ward received MRSA-Specific Antibiotics. Fortuin-de Smidt and co-authors (2015) conducted a study at three public hospitals in Gauteng, one of them being CMJAH, looking at the factors that are related to infections due to MRSA. They revealed that from the 36% of the cases that were identified as MRSA, directed treatment including MRSA-Specific Antibiotics were administered to only 59% of these cases. It is also important to note that death occurred in 62% of the MRSA cases that did not receive vancomycin treatment (Fortuin-de Smidt *et al.*, 2015). However, in this study, upon enquiring in the orthopaedic and vascular wards as to why these patients with a confirmed laboratory diagnosis of MRSA did not receive MRSA-Specific Antibiotics, it was suggested that in certain cases it was based on a patient's clinical symptoms and if the patient was recovering then their current empiric antibiotics would not be changed to MRSA-Specific Antibiotics, or if the patient was not receiving any antibiotics then MRSA-Specific Antibiotics would not be initiated.

In the orthopaedic ward, rifampicin was administered to eight out of the nine patients that received vancomycin for the treatment of MRSA. For MRSA bone or prosthetic joint infections, rifampicin can be used as an adjunctive therapy in combination with vancomycin (Kluytmans *et al.*, 2009) and at times rifampicin is also used an adjunctive therapy for *Staphylococcus aureus* infections in South Africa (Jansen van Rensburg *et al.*, 2012). Linezolid was used for only two patients in the orthopaedic ward. Although vancomycin has been seen as the “gold standard” for the treatment of MRSA, due to the development of resistance as well as pharmacokinetic and pharmacodynamics parameters, the use of vancomycin is being reviewed and replaced with alternative agents such as linezolid or daptomycin (Micek, 2007; Edwards *et al.*, 2014). Studies have thus been conducted to investigate the costs and clinical benefits of using these alternative agents as compared to vancomycin. Despite the higher cost of linezolid, studies have shown that linezolid may be more cost-effective than vancomycin for MRSA skin and soft tissue infections (Bounthavong *et al.*, 2009; Stephens *et al.*, 2013), and MRSA pneumonia (Machado *et al.*, 2005; Patel *et al.*, 2014).

As the WHO DDD can be used to monitor antibiotic usage in hospitals, the PDD of each antibiotic administered to each patient was calculated and compared to the WHO DDD. Only 39% of the PDD in vascular and 40% of the PDD in orthopaedic ward were equal and matched the WHO DDD. These results are similar to the results of other studies which compared antibiotic PDD and WHO DDD. A study performed by de With and co-authors at a university hospital, found that only 36% of the PDD were equal to the DDD (de With *et al.*, 2009). Similarly, another study compared the DDD with the PDD of antibiotics used at a university hospital reported that for many of the antibiotic classes, the DDD was not equal to the average PDD. However, the study suggests that in conjunction with using the WHO DDD every hospital should formulate a standard measure to monitor antibiotic usage (Muller *et al.*, 2006). The WHO acknowledges that the DDD is a unit of measurement for comparing drug utilization and DDD may differ from the PDD due to individual patient characteristics (World Health Organization Collaborating Centre for Drug Statistics Methodology, 2012).

5.5.2 NHLS Microbiology Data Review

The retrospective records review showed differing methods of capturing patients’ laboratory test results, thereby reflecting a lack of standard data capturing processes. The printouts of the NHLS laboratory test results were a reliable source of data; however, they were not always present in the patient records. The other sources of data in which patients' laboratory test results were recorded, such as written on tables or as notes, could not be classified as reliable sources as it was seen that often the results were incompletely recorded and important information was missing.

As the information present in the retrospective patient records regarding their laboratory test results was not always reliable, information obtained from the NHLS Corporate Data Warehouse Information Systems was used to obtain the detailed information. Several well-conducted and published studies relating to MRSA in South Africa have also obtained their data from the NHLS Corporate Data Warehouse Information Systems (Bamford *et al.*, 2011; Jansen van Rensburg *et al.*, 2012) and thus it can be seen as a reliable public sector database.

It was found that when a patient had a suspected infection, numerous specimens were taken and sent to the microbiology laboratory to be tested. The number of laboratory tests reported in this study represents only those laboratory tests that isolated MRSA. In the orthopaedic ward, the patients had a range of between one to ten with an average of three microbiology laboratory tests conducted that isolated MRSA. In the vascular ward, however, the patients had fewer repeat tests, with a range of one to four, with an average of two microbiology laboratory tests conducted that isolated MRSA.

To ensure the optimal management of patients, two-way communication has to occur between HCPs in the ward and the laboratory, in which the HCPs provide the laboratory with complete clinical information regarding the tests ordered per patient. This aids the laboratory in performing the correct tests, interpreting the results, and reducing the performance of unnecessary tests, thus decreasing costs, time and resource utilization (Georgiou *et al.*, 2011). These problems could be prevented and communication could be further improved if point of care testing were to be implemented in the wards in which PCR tests are conducted in the wards. Brenwald and co-authors (2010) conducted a study in which patients' nasal swabs were tested using the Xpert MRSA tests that were implemented in the wards using the Xpert MRSA tests that were implemented in the microbiology laboratory. It was found that on average the test results from the ward were available more than ten hours earlier that the test results from the laboratory (Brenwald *et al.*, 2010). A study by Parcell and Phillips (2014) showed another advantage of using the Xpert MRSA as point of care testing, in that it reduces the number of negative specimens that would be sent to the microbiology laboratory, thus enabling the negative test results to be available faster as well as reducing the work-load of the laboratory personnel.

Depending on the type of suspected infection, different types of specimens from different sites were taken and sent to the NHLS Microbiology Laboratory to be tested. From the tests that isolated MRSA in the orthopaedic ward, an equal number of fluid, irrigation fluid and tissue specimens were taken. This was not the case for the laboratory tests that isolated MRSA in the vascular ward as tissue specimens were most common, followed by pus swabs.

A study that investigated the antimicrobial susceptibility patterns of *staphylococcus aureus* isolates in KwaZulu-Natal found that from the MRSA isolates, 78.7% were from wound samples, 9.8% were from sputum and 3.3% were from otitis media (Shittu *et al.*, 2006).

5.6 Cost Analysis

When a patient is discharged from CMJAH, they do not receive an itemised bill with details regarding the costs of the antibiotics administered and laboratory tests conducted and no records of this costing information were available. CMJAH, along with many public hospitals in South Africa, uses the UPFS as a guide for billing patients. The UPFS implements a group fee approach rather than an itemised billing approach, as well as patients are billed and grouped according to their income. Thus, two patients receiving the same medical treatment may be billed at different rates (Department of Health, 2009). Hence the requirement for obtaining separate antibiotic and NHLS laboratory test costing databases to manually calculate each individual antibiotic and laboratory utilization cost per patient in this study.

Another reason as to why cost utilization calculations were performed for each antibiotic administered to each patient was because the dose, frequency and duration of antibiotics administered was not always standard. Although the NHLS data has standard costs per procedure, the cost of each laboratory test per patient has to be individually calculated as different procedures are conducted for each test.

5.6.1 Antibiotic Cost Calculations

Each patient received a different combination of antibiotics while in hospital and these antibiotics would change throughout their treatment. Thus, numerous calculations were conducted per patient. The sum of the cost of antibiotics administered per patient per day ranged from R42.56 to R1 695.04 with an average of R408.42 in the orthopaedic ward and R2.71 to R2 435.65 with an average of R462.51 in the vascular ward.

In the orthopaedic ward it was interesting to note that although 56.41% of the antibiotics administered were Empiric Antibiotics, only 24% of the daily cost of antibiotics administered was due to Empiric Antibiotics and 60% of the daily cost of antibiotics administered was due to MRSA-Specific Antibiotics administered, which accounted for only 34.62% of all the antibiotics administered. However, in the vascular ward, 19.27% of the antibiotics administered were MRSA-Specific Antibiotics and 14% of the daily cost of antibiotics administered was due to MRSA-Specific Antibiotics administered. The lower cost of MRSA-Specific Antibiotics in the vascular ward could due to the fact that linezolid, which has an average weighted price (contract) of R282.25 per 600 mg tablet, was not administered to any of the patients in the vascular ward.

When analysing the cost and utilization of individual antibiotics to the patients, the average daily cost of an antibiotic administered in the orthopaedic ward ranged from R0.41 for metronidazole to R564.49 for linezolid, while the average daily cost of an antibiotic administered in the vascular ward ranged from R0.30 for metronidazole tablets to R460.41 for ertapenem IVI.

Although the same antibiotic costing database was used when performing calculations for the orthopaedic and vascular wards, the average daily cost of an antibiotic differed between the two wards, as different doses and durations of treatment were used. For example, the average weighted price (contract) of vancomycin 1g vial is R46.97. The average daily cost of vancomycin was R115.29 in the orthopaedic ward and R77.50 in the vascular ward. The average number of days that antibiotics were administered also differed, as the average number of days that a patient received vancomycin was nine days in the orthopaedic ward and three days in the vascular ward.

Due to the restricted use and high cost of linezolid, only two patients in the orthopaedic ward received linezolid and none of the patients in the vascular ward received linezolid. Despite the cost of linezolid being higher than the cost of vancomycin, studies have shown that linezolid may be more cost-effective than vancomycin for patients with MRSA (Machado *et al.*, 2005; Stephens *et al.*, 2013).

5.6.2 NHLS Laboratory Tests Cost Calculations

Depending on the steps taken for each laboratory test, the cost per test was calculated. The costs per step also differed slightly depending on the type of specimen being tested. Each laboratory test commences with one microscopy step which has a standard cost of either R36.93 or R38.41. Each culture and sensitivity step conducted thereafter had a separate cost.

Therefore, once calculated, the cost per NHLS laboratory test that isolated MRSA ranged from R118.38 to R592.80 with an average of R335.09 per test in the orthopaedic ward and from R168.37 to R660.40 with an average of R373.03 per test in the vascular ward. Studies have shown that the Xpert MRSA tests are more expensive than the Conventional Culture Method (French, 2009; Havill, 2010; Marlowe *et al.*, 2011), however, in both the wards in this study, the average cost of a Conventional Culture test that isolated MRSA was more expensive than the cost of one Xpert MRSA test (R307.52). Although the difference in cost may seem slight, it should be highlighted that if the Xpert MRSA test produces MRSA-positive results, further antibiotic sensitivity tests would still need to be conducted and would thus further increase the cost of using the Xpert MRSA tests.

As established from the retrospective records, patients had multiple duplicated microbiology laboratory tests conducted. However, one could assume that the HCPs were unaware of the cost implications of numerous tests. The total cost of laboratory tests that isolated MRSA per patient ranged from R260.13 to R3 184.23 with an average of R921.51 per patient in the orthopaedic ward and from R168.37 to R1 492.05 with an average of R565.97 per patient in the vascular ward.

5.6.3 Cost Calculations of Antibiotic Utilization plus NHLS Laboratory Tests per Patient

A complete account of the antibiotics administered and the NHLS laboratory tests conducted that isolated MRSA per patient in the study population was calculated. The total sum of the Antibiotic Utilization Cost and the total of NHLS cost per patient ranged from R567.31 to R12 583.15 in the orthopaedic ward and from R45.06 to R16 199.18 in the vascular ward. Each patient's total antibiotic utilization cost and total NHLS cost was then added to obtain a combined total cost per ward. The antibiotic utilization costs were responsible for the majority of the costs in the vascular ward (80.91%) and in the orthopaedic ward (76.04%).

Many studies examining the additional patient management costs for a patient with an MRSA infection included other costs such as hospital stay costs, isolation costs, labour costs, screening costs and PPE costs. Studies also looked at the cost-effectiveness of using PCR tests instead of Conventional Culture tests and the sensitivity and specificity of the PCR tests as compared to the Conventional Culture tests (Gould, 2006; Wassenberg *et al.*, 2010; Li *et al.*, 2012; Tübbicke *et al.*, 2012a). However, when calculating the management costs of a patient with an MRSA infection in this study, only the costs of antibiotics and microbiology laboratory tests that isolated MRSA were included, as it was assumed that all other costs would remain constant, irrespective of the testing methods. Due to the fact that the Xpert MRSA tests were not yet implemented in the study area, the cost-effectiveness (the cost of the additional clinical benefit), sensitivity and specificity could not be measured.

5.7 Decision-Tree-Analytic Models

International studies have developed decision-tree-analytic models to compare the costs of the Conventional Culture Method and the new PCR tests for MRSA. However, due to the South African public healthcare setting being different as compared to other healthcare settings, in areas such as access to healthcare and limited availability of resources (Ataguba *et al.*, 2011) as well as differences in the implementation of surveillance and record keeping systems (Nyasulu *et al.*, 2012), the results obtained from these international studies are not necessarily true to the South African context and cannot be directly applied to the public healthcare settings in South Africa.

Therefore, to depict the current management pathways of patients with a suspected infection, decision-tree-analytic models were developed for each ward in the study. Although the patient management pathways presented may not appear to follow standard clinical practice, they were derived from the observations conducted and data obtained from the patients' retrospective records. A theoretical arm was added to each tree to evaluate the effect of implementing the Xpert MRSA tests in the current clinical settings. In addition, these models were then run depicting a theoretical situation of patients having an equal chance of receiving either management pathway, by using variables to assign equal probabilities to each pathway.

The input parameters for the decision-tree-analytic models formulated in this study were delivered from the data obtained in this study from the patients' retrospective records, observations and the cost analysis. In comparison to other studies that developed similar decision-tree-analytic models, some of these studies obtained their input parameters from conducting peer-reviewed literature searches (Brown *et al.*, 2010; Hübner *et al.*, 2012; Tübbicke *et al.*, 2012a; Tübbicke *et al.*, 2012b), while other studies obtained their input parameters from conducting actual research and trials on both the culture and Xpert MRSA tests (Li *et al.*, 2012).

The total cost of each possible management pathway for a patient with a suspected infection was calculated. It is interesting to note the wide range and high cost of these management pathways in both wards. If the Xpert MRSA tests were to be implemented in the current clinical settings, it is uncertain as to what the exact testing procedure would be, as the Xpert MRSA test results only reveal whether the patient is MRSA-positive or not. Hence, if a patient is MRSA-positive, further antibiotic sensitivity tests would need to be conducted. Therefore a variation in costs occurred as the potential situations were depicted. Several studies have been conducted introducing the implementation of the Xpert MRSA tests. However, a consistent clinical testing methodology could not be derived from these studies. Some studies involved comparing the sensitivity and specificity of the Xpert MRSA tests to the Conventional Culture Method thus using both of these testing methods concurrently (Andersen *et al.*, 2010; Li *et al.*, 2012). While another study suggested that the PCR test could be conducted first and thereafter the Conventional Culture test would only be conducted if the PCR test reflected a positive MRSA result (Tübbicke *et al.*, 2012a). Furthermore, studies report that when using PCR tests, the Conventional Culture Method should be used as the final confirmation method (Wassenberg *et al.*, 2010; Li *et al.*, 2012). This is also in accordance with the Xpert MRSA package insert which stipulates that simultaneous tests using the culture method are required to obtain information regarding antibiotic susceptibility (Cepheid, 2012).

Ranking analysis was then performed, which evaluated the optimal strategy with the lowest cost. Despite the numerous differences found between the orthopaedic and vascular wards, the optimal strategy in the current clinical strategy in both of these wards was when Empiric Antibiotics were administered and a Specimen For MRSA was simultaneously taken. However, if the Xpert MRSA tests were to be implemented in the current settings, the Xpert MRSA strategy was the optimal strategy in the orthopaedic ward, but was the most expensive strategy in the vascular ward. Li and co-authors also developed a decision-tree-analytic model using TreeAge to compare new strategies of implementing the Xpert MRSA tests with the current Conventional Culture strategy for screening hospital patients and found that the Xpert MRSA was the optimal strategy. These findings from Li and co-authors are in line with the results obtained for the orthopaedic ward in this study (Li *et al.*, 2012).

Furthermore, Brown and Paladino developed a decision-tree-analytic model on TreeAge, which included the effects of implementing the Xpert MRSA test on mortality and antibiotic usage and concluded that the current usage of empiric antibiotics is more costly than the costs of using the Xpert MRSA tests overall (Brown *et al.*, 2010). Another study also formulated decision-tree-analytic models to evaluate the costs and effects that PCR tests would have on antibiotic usage for MRSA. This study reported that compared to empiric antibiotics that are administered without first having PCR test results, antibiotics administered which are guided by a PCR test result are more cost-efficient and lead to targeted antibiotic use for MRSA (Hübner *et al.*, 2012). Although these studies evaluated the influence of MRSA tests on antibiotic usage for MRSA, they did not include a comparison arm reflecting the costs and consequence of the culture method on antibiotic usage. Therefore, this study investigated the costs and consequences of both the culture method and Xpert MRSA tests on antibiotic usage for a patient with suspected or confirmed MRSA.

5.8 Limitations of the Study

During this study, numerous challenges were faced and those that could not be overcome or changed may be seen as limitations of this study. The main limitations that affected this study are discussed below.

5.8.1 Data Capturing

The study was conducted at CMJAH, which is one of the main public sector hospitals in Johannesburg, South Africa. Within the wards included in the study, there was no electronic system for capturing data.

5.8.1.1 Patient Records

The HCPs hand-wrote notes into the patient records and these notes were the only form of patient data recorded and available. Therefore, the patient records are based purely on the manner in which they were written into the patient records. Within these records were written notes from specialists, doctors, interns, nurses and other HCPs. Many limitations of this current manual system of record-keeping were identified while viewing the retrospective patient records.

The quality and quantity of the notes written in the patient records were a major limitation and greatly impacted this study. When viewing the retrospective patient records, all the required information was recorded from the many different types of records in the patient records such as the doctors' notes, discharge sheets, prescription charts, administration charts and laboratory test printouts. However, when analysing and comparing the data, the type of record that seemed the most valid was used as the standard record for that set of information. For example, the discharge sheet was used to obtain the diagnosis of each patient.

When obtaining information regarding medications prescribed and administered to a patient, the doctors' prescription charts and the nurses' administration charts were used. However, a limitation of both these types of charts was that they were not always completely filled in and therefore a lot of data was missing. On the doctors' prescription charts, some prescriptions were not complete as to strength of medication and route of administration, or other information was missing. Another challenge was that in many instances there was no date and signature in the column which indicates when the medication was discontinued. Other problems were that in some records there was more than one prescription chart running at the same time and the same or similar antibiotics had been prescribed. Overall, the nurses' administration charts were more thoroughly completed than the doctors' prescription charts. However, the spaces on the nurses' prescription charts were small and thus difficult at times to read clearly. For both types of charts, it was difficult to read some of the handwriting and thus assumptions had to be made. When looking at the doctors' prescription charts in conjunction with the nurses' administration charts, at times there were antibiotics written on the doctor's prescription chart but not present on the nurse's administration chart. This could be due to many reasons such as doctors prescribing an out of stock antibiotic. For each patient, information regarding antibiotics was recorded from both the doctors' prescription charts and the nurses' administration charts. Information regarding antibiotics prescribed and administered was also recorded from the doctors' notes, but in certain cases the information in the doctors' notes did not match up with the prescription and administration chart

information. Therefore, in the event of any discrepancy the information on nurses' prescription charts was used, as it was chosen as the more reliable sore of information.

There was also inconsistency in the information written in patient records. For example, in the doctor's notes the age of a patient would vary. Therefore, to standardise the patient information, the patient's discharge sheet was used to obtain the diagnosis, operations performed, admission date and discharge date. The age and gender of a patient was obtained from data received from the NHLS Information System.

Within the patient records, the NHLS printouts of laboratory tests performed were not always present. In some records the results of the NHLS laboratory tests were written down in the doctors' notes or at the bottom of the flow chart and they contained the written values of other tests conducted (Hb, Na, K, Cl, etc.). In some of the records for the vascular ward patients, A4 printed Tables could be found with headings for date, laboratory test number, Specimen, Identification and Sensitivity, on which the different laboratory test details were written down; or there were printed pages headed *Lab Tests from MY PATIENT RESULTS,* on which were noted details of the laboratory tests. The limitation that was identified when the laboratory test details and results were hand-written was that not all the information was written down and it was unclear whether the results were provisional or final and whether the date indicated the date that the specimen was taken or the date of the final report. The printed out pages from *Lab Tests from MY PATIENT RESULTS* had all the required information but they were present only in a few of the records. When viewing the records, laboratory test information was recorded from all of these sources present in a patient's record. However, due to the various methods by which the laboratory tests were recorded in the records and that no consistent method was used to record them in all the records, the data received from the NHLS Information System regarding the laboratory tests conducted which isolated MRSA was the only data that was used for the laboratory tests for the study.

When viewing the retrospective patient records, it seemed as if pages were missing. For example, when looking at the doctors' notes, there would be a blank period of dates for which there were no notes. This could be due to the actual page containing the doctors' notes for that period going missing in the ward, or the page being lost when the records were scanned onto microfilm in the Records Room.

5.8.1.2 Medical Records Room

The Medical Records Room at CMJAH uses a tedious manual system with numerous limitations for storing, accessing and viewing patient records. When the scanning of patient records onto microfilm takes place, the pages are at times not scanned correctly and when

viewing the records, pages overlapped, were upside-down or blurred, thus making them difficult to read. Time had to be spent adjusting the viewer and trying to decipher the notes. Pages were often missing and had not always been scanned in the correct order. Only two working microfiche viewers were available and at times there was a delay if staff needed to view a record, or if another researcher was present, turns had to be taken.

The manual system in the Medical Records room is slowly being replaced by an electronic computerised system. However, as there are a limited number of computers, access was allowed for only a few hours in the morning before the staff arrived at work. For both the manual and electronic system, taking pictures, printing or any other means of saving or copying the data was not permitted and thus all required information had to be handwritten on the case report forms.

Once the required information had been retrieved from the patient records in the study population, the data was typed up and missing information was identified. Missing information was a limitation in this study and was dealt with in various ways. Doctors were consulted to explain certain concepts and trends that were noticed and where possible and acceptable, assumptions were made to try and reduce the amount of missing information.

5.8.1.3 Main Dispensary

The main dispensary at CMJAH also works on a manual system and there is currently no electronic system for dispensing data. This was a limitation as if this data were available it would have greatly assisted in analysing the dispensing of antibiotics to patients with MRSA. However, as this data was not available, the retrospective patient records had to be used. An electronic dispensing system would also greatly benefit the overall communication and dispensing process between the wards and the dispensary.

5.8.2 Protocols

Within the dispensary there were no written protocols that were strictly adhered to for the dispensing of antibiotics to inpatients. The protocols may have been formulated, but the pharmacists may not be aware of them and are thus not being followed. This is a limitation as there is no standardisation of the dispensing of antibiotics to inpatients and thus it was difficult to formulate clear management pathways as it was stated and observed in the retrospective patient notes that most dispensing is done on a per case basis. Within the wards that were observed in the study there were also no written protocols being followed with regard to antibiotic prescribing as it was stated that this was based on clinicians' preferences and other factors. This poses a limitation as there was no standard against which to compare the current clinical practice.

5.8.3 Antibiotic Stewardship

Currently there is also no active antibiotic stewardship programme implemented between the main dispensary and the wards included in the study at CMJAH. The absence of an antibiotic stewardship programme in this setting was a limitation, as in the records it could be seen that there was no effective communication between the doctors in the wards and pharmacist in the dispensary. This lack of communication could cause delayed antibiotic treatment, which should be avoided in order to ensure the optimal treatment of patients. If an antibiotic stewardship programme were to be initiated in this setting, it would have numerous benefits and would have a different effect on the implementation of the Xpert MRSA tests.

As CMJAH is an academic hospital, there are various levels of HCPs that consult with the patients. The medical interns are sometimes unsupervised and at times they have to wait for a senior doctor to authorise certain procedures and prescriptions. The interns also rotate to different wards, making it difficult to follow up on a patient's progress.

5.8.4 Resources

CMJAH as a public sector hospital often has to deal with basic and limited resources as well as medications being out of stock. This has a negative impact on patient care and was a limitation to this study as patient management pathways were affected when antibiotics were out of stock.

5.8.5 Number of MRSA cases at CMJAH in 2013

This study requested and received data regarding all the MRSA cases identified at CMJAH from 01 January 2013 to 31 December 2013. However, the limited number of patients identified with MRSA in the orthopaedic and vascular ward could be seen as a limitation as these numbers were used to populate the decision-tree-analytic models and thus could have impacted on the outcomes of the models.

Although international studies have been conducted on a larger scale and have larger sample sizes, the unique outcomes obtained from the models in this study are not necessarily due to the small sample size, but rather due to the manner in which this hospital is managed as compared to other hospitals. If a larger number of MRSA cases were identified at CMJAH and met the inclusion criteria of this study, the outcomes obtained from these models would have had more certainty.

Therefore, to address this limitation and the impact that it could have had on the outcomes of the models, equal decision-tree-analytic models were developed and analysed to evaluate

the outcome of using various theoretical probabilities for the number of patients identified with MRSA.

5.9 Assumptions

Certain assumptions were made during this study and they are discussed below.

The two main costs associated with performing the Xpert MRSA test are the Xpert MRSA kit and the Gene Xpert System. Currently the NHLS Microbiology at CMJAH has the Gene Xpert System, as it is being used to perform other assays. Therefore, when calculating the cost of implementing the Xpert MRSA tests at CMJAH it was assumed that there is currently available capacity to perform the Xpert MRSA tests in the Gene Xpert Systems already present at the NHLS Microbiology Laboratory. Hence, no additional capital cost for purchasing the Gene Xpert System was included and only the cost of the Xpert MRSA kits was included. When calculating the costs of implementing the Xpert MRSA tests it was also assumed that each patient would have only one Xpert MRSA test.

When analysing the antibiotics that were administered to the patients in the study population, assumptions were made in order to limit the amount of missing data and to perform the cost calculations. For IV administrations it was assumed that there was no vial-sharing and that a minimum of one of the smallest quantity of vials available was used if the dose administered was less than one vial. In cases where the same antibiotic was written several times, but with some of them written incompletely or lacking information, the cases that had missing information were ignored as it was assumed that it had been incorrectly, or not completely, although ultimately the patient had received the antibiotic at least once. When an antibiotic was written down only once for a patient but there was insufficient information given, doses were not assumed as standard doses, thus patterns could not be derived from what had been administered. Information that was completely missing was dealt with by interpolation using the information that was available.

6. CONCLUSION

The current management pathways for a patient with a suspected MRSA infection in the orthopaedic and vascular wards at CMJAH were formulated and costed by qualitative and quantitative research methods. Using the decision-tree-analytic models constructed, the costs of these management pathways were then compared to theoretical management pathways of implementing the Xpert MRSA tests in the current clinical setting.

From the qualitative observations conducted in the two wards, the NHLS Microbiology Laboratory and antibiotic designated area of the main dispensary at CMJAH, it was found that the communication between these three areas of the hospital needs to be improved to enhance the management of patients with a suspected or confirmed MRSA infection.

The findings from the qualitative observations were strengthened by the quantitative aspects of the study that followed. The retrospective utilization and records review highlighted the inconsistent utilization of antibiotics and the multiple NHLS laboratory tests conducted that isolated MRSA in the study population. The cost analysis emphasised that although unnecessary and repeated NHLS laboratory tests for MRSA were conducted and contributed to the costs, it was actually the cost of the numerous antibiotics administered that accounted for the majority of the costs of the patients in the study population.

Based on the qualitative and quantitative findings, a single management pathway for a patient with a suspected MRSA infection could not be deduced and thus the various pathways that occurred were depicted in the decision-tree-analytic models per ward. The ideal pathway for a patient with a suspected MRSA infection in the current clinical setting in the orthopaedic and vascular wards is when a Specimen is Sent For MCS and Empiric Antibiotics are administered concurrently. It was found that if the Xpert MRSA tests were implemented in the orthopaedic ward, the optimal strategy for a patient with a suspected infection would be to first take a Specimen For Xpert MRSA testing. However, if the Xpert MRSA tests were implemented in the vascular ward, the most expensive strategy for a patient with a suspected infection would be to first take a Specimen For Xpert MRSA testing.

Therefore, before new MRSA testing methods are introduced in the hospital, it is suggested that the current practices and pathways for MRSA should be further evaluated and improved.

7. RECOMMENDATIONS AND FUTURE RESEARCH

This study aimed to investigate the cost of the management pathways associated with using the current Conventional Culture Method versus the cost of management pathways that would follow if the new PCR testing for MRSA were to be implemented, in order to give a recommendation as to whether or not the of Xpert MRSA tests should be implemented at CMJAH. However, by conducting this study, various additional recommendations were identified.

As the two wards that were involved in the study still use a manual paper-based system for recording patient notes and prescriptions, it is recommended that an electronic recording system be introduced, as it would provide numerous benefits to both HCPs and patients. The antibiotics designated area of the main dispensary of CMJAH also uses a manual paper-based dispensing system, thus, if the current system were to be replaced by an electronic computer-based dispensing system, there would be improved control of antibiotic utilization. Electronic systems would also improve the communication between the HCPs in the wards, the dispensary and the microbiology laboratory, which would lead to a reduction in the number of MCS tests conducted, a decrease in the waiting period for the MCS results, prompt administration of antibiotics and enhanced patient management.

Standard protocols and guidelines regarding managing patients with a suspected and confirmed infection and antibiotic prescribing and dispensing should be formulated and followed in the wards and dispensary. It is recommended that a strong Antibiotic Stewardship programme be developed and implemented at CMJAH which should include a multidisciplinary collaboration between the dispensary, the wards and the microbiology laboratory as well as follow the standards that are being set by the National Department of Health.

To assist in the optimal use of scarce resources, it is recommended that HCPs should become cost conscious and be made aware of the financial implications of their daily practices when managing patients.

It is recommended that the current system used in the Hospital's Medical Record Room should be reviewed and updated to enable safe storage and easy access to retrospective patient records. If the various areas of the hospital were to start using electronic means of recording patient data it would be simple to update the current system in records room; if not, the patient data should be entered onto a computerised searchable database as it would aid gathering information for surveillance, utilization trends and future research.

As this study focused only on the direct antibiotic and laboratory test utilization costs of implementing the Xpert MRSA tests at CMJAH, it is recommended that once the current practices and management pathways for a patient with a suspected or confirmed MRSA infection are improved, future research should be conducted using TreeAge decision-tree-analytic models to assess the cost-effectiveness and patient outcomes associated with implementing the Xpert MRSA tests at CMJAH.

8. APPENDICES

APPENDIX 1

8.1 Human Research Ethics Committee: Clearance Certificate

M130543

R14/49 Ms Sadiyya Ahmed-Hassen

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130543

NAME: (Principal Investigator)	Ms Sadiyya Ahmed-Hassen
DEPARTMENT:	Department of Pharmacy & Pharmacology Medical School
PROJECT TITLE:	A South African cost Analysis of Polymerase Chain Reaction Testing versus Conventional Culture Screening for Methicillin-Resistant Staphylococcus Aureus (revised title)
DATE CONSIDERED:	31/05/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Mrs Shirra Moch
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 31/07/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Amen
Principal Investigator Signature

06/08/2013
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

8.2 Letter of Research Permission

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. L. Mngomezulu
(011): 488-3793
(011) 488-3753
25 July 2013

Sadiyya Ahmed-Hassen
Department of Pharmacy and Pharmacology
University of Witwatersrand

Dear Sadiyya

RE: "A South African cost Analysis of Polymerase Chain Reaction Testing versus Conventional Culture Method in Screening for the Methicillin- Resistant Staphylococcus Aureus"

Permission is granted for you to conduct the above research as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic hospital will not in anyway incur or inherit costs as a result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall be observed at all times.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the Head of Department and Unit Manager or Sister in Charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Ms. G. Bogoshi
Chief Executive Officer
25/7/2013

8.3 Data Collection Sheets

8.3.1 Clinical Ward Observation Data Collection Sheet

Clinical Ward Observations	**Ward :** **Date:**
Ward Rounds	
HCP-Patient interaction	
Antibiotics	
Infection Control	
Isolation	
Taking Specimens	
Suspected Infection	
Confirmed Infection	
Pre/Post-Operative Care	
Patient Notes	
Other	

8.3.2 Microbiology Laboratory Observation Data Collection Sheet

NHLS Microbiology Laboratory					Date:
CONVENTIONAL CULTURE METHOD					
	Planting	**Microscopy**	**Culture**	**Picking**	**Sensitivity**
Equipment Required					
Procedure					
Hands-On Time					
Incubation Time					
Recording of Results					
Other					

8.3.3 Antibiotic Dispensary Observation Data Collection Sheet

Antibiotics at the Main Dispensary	**Date:**
General policy for dispensing antibiotics	
Policy for antibiotics kept as ward stock	
Policy for antibiotics dispensed on a per-patient basis	
Antibiotics which require Motivation	Vancomycin: Linezolid: Carbapenems:
Antibiotics which require Authorisation	Vancomycin: Linezolid: Carbapenems:
Antibiotics which require Laboratory Results	Vancomycin: Linezolid: Carbapenems:
Current Antibiotic Stewardship	
Other	

8.4 Individual Patient Case Report Form

PATIENT DETAILS							
ALLOCATED PATIENT #	GENDER	AGE	ADMISSION DATE	DISCHARGE DATE	DIAGNOSIS / ICD10 CODE	OPERATION	TEMP

ANTIBIOTICS							
DATE	DRUG	DOSAGE FORM	STRENGTH	DOSE	FREQUENCY	DURATION	INSTRUCTIONS

LABORATORY RECORDS FOR INFECTION													
Lab #	Date Taken	Date of Report	Specimen	Test	G+C	Culture Results		Remark	Entered	Antibiotic [S]	E-Strip	Remark	Entered
						Aerobic	Anaerobic						

DOCTOR'S NOTES	ADDITIONAL INFORMATION

8.5 Costing Information

8.5.1 Antibiotic Costing Information

Table 29: Summary of the Database Medsas-contract-prices-INN-ATC 2013 Reflecting the Antibiotics used in the Orthopaedic Ward

Item description (Medsas)	Average weighted price (contract)	Depot price (without mark-up)
AMOXYCILLIN AND CLAVULANIC ACID TABLETS 500MG AND 125MG;15'S	R 17.33	R 20.90
AMOXYCILLIN AND CLAVULANIC ACID TABLETS 875MG AND 125MG;10'S	R 13.54	R 14.93
AMOXYCILLIN SODIUM AND POTASSIUM CLAVULANATE FOR INJECTION; 1000MG AND 200MG/VIAL	R 12.52	R 13.50
AMOXYCILLIN SODIUM AND POTASSIUM CLAVULANATE FOR INJECTION; 500MG AND 100MG/VIAL	R 7.16	R 7.16
GENTAMICIN INJECTION: 20MG PER 2ML; 2ML	R 3.99	R 3.99
RIFAMPICIN CAPSULES 600MG;100'S	R 84.81	R 97.47
VANCOMYCIN POWDER FOR INJECTION USP; 1000MG/VIAL	R 46.97	R 52.17
CLOXACILLIN SODIUM FOR INJECTION: 500MG/VIAL	R 5.24	R 6.58
CLOXACILLIN SODIUM CAPSULES 500MG; 100'S		R 190.98
CEFOXITIN SODIUM FOR INJECTION: 1GM	R 20.52	R 21.46
CEFAZOLIN SODIUM INJECTION: 1G/VIAL	R 4.00	R 4.65
LINEZOLID TABLETS 600MG;10'S	R 2,822.45	R 2,822.45
ERTAPENEM SODIUM POWDER FOR INJECTION 1G;20ML	R 368.33	R 368.33
METRONIDAZOLE TABLETS PATIENT READY PACK; 400MG;21'S	R 2.85	R 2.85
CIPROFLOXACIN TABLETS 500MG; 10'S	R 4.59	R 4.86
CEFTAZIDIME FOR INJECTION: 2G PER VIAL	R 60.00	R 60.00
CEFTAZIDIME FOR INJECTION: 1G PER VIAL	R 32.74	R 32.74

Table 30: Summary of the Database Medsas-contract-prices-INN-ATC 2013 Reflecting the Antibiotics used in the Vascular Ward

Item description (Medsas)	Average weighted price (contract)	Depot price (without mark-up)
VANCOMYCIN POWDER FOR INJECTION USP; 1000MG/VIAL	R 46.97	R 52.17
AMOXYCILLIN SODIUM AND POTASSIUM CLAVULANATE FOR INJECTION; 1000MG AND 200MG/VIAL	R 12.52	R 13.50
CEFAZOLIN SODIUM INJECTION: 1G/VIAL	R 4.00	R 4.65
CLARITHROMYCIN TABLETS 500MG; 14'S	R 26.87	R 30.80
RIFAMPICIN INJECTION INTRAVENOUS; 300MG/VIAL		R 157.21
PIPERACILLIN 4G AND TAZOBACTAM 500MG INJECTION; POWDER FOR RECONSTITUTION IN 50ML VIAL	R 60.00	R 60.00
CEFEPIME INJECTION; 1G/VIAL	R 20.46	R 20.46
CEFEPIME INJECTION; 2G/VIAL	R 38.91	R 42.91
MEROPENEM TRIHYDRATE ANHYDROUS INJECTION; 500MG/VIAL	R 63.86	R 63.86
MEROPENEM TRIHYDRATE ANHYDROUS INJECTION; 1G/VIAL	R 125.95	R 125.95
ERTAPENEM SODIUM POWDER FOR INJECTION 1G;20ML	R 368.33	R 368.33
AMOXYCILLIN AND CLAVULANIC ACID TABLETS 500MG AND 125MG;15'S	R 17.33	R 20.90
AMOXYCILLIN AND CLAVULANIC ACID TABLETS 875MG AND 125MG;10'S	R 13.54	R 14.93
GENTAMICIN INJECTION: 20MG PER 2ML; 2ML	R 3.99	R 3.99
CLOXACILLIN SODIUM FOR INJECTION: 500MG/VIAL	R 5.24	R 6.58
METRONIDAZOLE INTRAVENOUS INFUSION 500MG/ML; 100ML	R 5.37	R 5.36
IMIPENEM AND CILASTATIN SODIUM FOR INJECTION :500MG AND 500MG;VIAL; 1'S	R 47.05	R 56.75
CEFTAZIDIME FOR INJECTION: 1G PER VIAL	R 32.74	R 32.74
AMIKACIN SULPHATE INJECTION: 250MG PER 2ML; 2ML	R 6.87	R 6.87
CEFUROXIME SODIUM FOR INJECTION: 750MG PER VIAL	R 7.84	R 8.86
CO-TRIMOXAZOLE TABLETS :TRIMETHOPRIM 80MG; SULPHAMETHOXAZOLE 400MG; 100'S	R 12.68	R 12.68
CLOXACILLIN SODIUM CAPSULES 500MG; 100'S		R 190.98
AMOXYCILLIN TRIHYDRATE CAPSULES 500MG; 100'S	R 20.41	R 27.00
CLINDAMYCIN PHOSPHATE INJECTION: 600MG PER 4ML	R 10.49	R 10.93
METRONIDAZOLE TABLETS 400MG; 100'S	R 10.13	R 12.54
CIPROFLOXACIN TABLETS 500MG; 10'S	R 4.59	R 4.86
CIPROFLOXACIN INJECTION 2MG/ML; 100ML	R 31.09	R 31.09

8.5.2 NHLS Laboratory Test Costing Information

Table 31: NHLS List of Prices of the Different Steps Used for the Laboratory Tests Conducted that Isolated MRSA in the Study Population in the Orthopaedic Ward

TEST CODE	TARIFF CODE	TARIFF_DESC	PRICE (R)
CULTI	0120	ANAEROBE CONFIRMATORY SCREEN	34.01
CULFL	0120	ANAEROBE CONFIRMATORY SCREEN	34.01
CULTI	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULFL	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULPU	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULPU	0326	BIOCHEM ID BACTERIUM ABRIDGED	24.78
CULFL	0327	BIOCHEM ID BACTERIUM EXTENDED	94.19
CULTI	0240	CULTURE AEROBIC	47.44
CULFL	0240	CULTURE AEROBIC	47.44
CULPU	0240	CULTURE AEROBIC	47.44
CULPU	0240	CULTURE AEROBIC	49.34
CULTI	0245	CULTURE ANAEROBIC	34.01
CULFL	0245	CULTURE ANAEROBIC	34.01
CULTI	0025	DISC SENSITIVITY (PER ORG)	60.17
CULFL	0025	DISC SENSITIVITY (PER ORG)	60.17
CULPU	0025	DISC SENSITIVITY (PER ORG)	60.17
CULPU	0025	DISC SENSITIVITY (PER ORG)	62.58
CULTI	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULFL	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULPU	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULPU	0080	MIC MBC KILL (MIC OR TUBE)	95.43
CULTI	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULFL	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULPU	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULPU	0331	MICROSCOPY ONLY STAINED PREP	38.41
CULTI	0162	RAPID AUTOMATED ANTIBIOTIC SUSCEPTIBILIT	127.99
CULFL	0162	RAPID AUTOMATED ANTIBIOTIC SUSCEPTIBILIT	127.99
CULFL	0161	RAPID AUTOMATED BACTERIAL IDENTIFICATION	112.83
CULTI	0161	RAPID AUTOMATED BACTERIAL IDENTIFICATION	112.83

Table 32: NHLS List of Prices of the Different Steps Used for the Laboratory Tests Conducted that Isolated MRSA in the Study Population in the Vascular Ward

TEST CODE	TARIFF CODE	TARIFF_DESC	PRICE (R)
CULFL	0120	ANAEROBE CONFIRMATORY SCREEN	35.37
CULPU	0120	ANAEROBE CONFIRMATORY SCREEN	34.01
CULTI	0120	ANAEROBE CONFIRMATORY SCREEN	34.01
CULTI	0120	ANAEROBE CONFIRMATORY SCREEN	35.37
CULBA	0160	AUTOMATED BLD CULT AEROBIC GROWTH	108.79
CULBA	0170	AUTOMATED BLOOD CULT ANAEROBIC GROWTH	104.61
CULBA	0326	BIOCHEM ID BACTERIUM ABRIDGED	24.78
CULBA	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULFL	0326	BIOCHEM ID BACTERIUM ABRIDGED	24.78
CULPU	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULPU	0326	BIOCHEM ID BACTERIUM ABRIDGED	24.78
CULSP	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULST	0326	BIOCHEM ID BACTERIUM ABRIDGED	24.78
CULST	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULTI	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULTI	0326	BIOCHEM ID BACTERIUM ABRIDGED	24.78
CULUR	0326	BIOCHEM ID BACTERIUM ABRIDGED	23.83
CULPU	0327	BIOCHEM ID BACTERIUM EXTENDED	94.19
CULPU	0327	BIOCHEM ID BACTERIUM EXTENDED	97.96
CULSP	0327	BIOCHEM ID BACTERIUM EXTENDED	94.19
CULTI	0327	BIOCHEM ID BACTERIUM EXTENDED	94.19
CULUR	0327	BIOCHEM ID BACTERIUM EXTENDED	94.19
CULCT	0240	CULTURE AEROBIC	49.34
CULFL	0240	CULTURE AEROBIC	49.34
CULPU	0240	CULTURE AEROBIC	47.44
CULPU	0240	CULTURE AEROBIC	49.34
CULSP	0240	CULTURE AEROBIC	47.44
CULTI	0240	CULTURE AEROBIC	47.44
CULTI	0240	CULTURE AEROBIC	49.34
CULFL	0245	CULTURE ANAEROBIC	35.37
CULPU	0245	CULTURE ANAEROBIC	34.01
CULPU	0245	CULTURE ANAEROBIC	35.37
CULTI	0245	CULTURE ANAEROBIC	34.01
CULTI	0245	CULTURE ANAEROBIC	35.37

CULST	0275	CULTURE FOR STAPH AUREUS	17.7
CULST	0275	CULTURE FOR STAPH AUREUS	17.02
CULBA	0025	DISC SENSITIVITY (PER ORG)	62.58
CULBA	0025	DISC SENSITIVITY (PER ORG)	60.17
CULFL	0025	DISC SENSITIVITY (PER ORG)	62.58
CULPU	0025	DISC SENSITIVITY (PER ORG)	60.17
CULPU	0025	DISC SENSITIVITY (PER ORG)	62.58
CULSP	0025	DISC SENSITIVITY (PER ORG)	60.17
CULTI	0025	DISC SENSITIVITY (PER ORG)	60.17
CULTI	0025	DISC SENSITIVITY (PER ORG)	62.58
CULUR	0025	DISC SENSITIVITY (PER ORG)	60.17
CULBA	0080	MIC MBC KILL (MIC OR TUBE)	95.43
CULBA	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULFL	0080	MIC MBC KILL (MIC OR TUBE)	95.43
CULPU	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULPU	0080	MIC MBC KILL (MIC OR TUBE)	95.43
CULSP	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULTI	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULTI	0080	MIC MBC KILL (MIC OR TUBE)	95.43
CULUR	0080	MIC MBC KILL (MIC OR TUBE)	91.76
CULBA	0331	MICROSCOPY ONLY STAINED PREP	38.41
CULBA	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULFL	0331	MICROSCOPY ONLY STAINED PREP	38.41
CULPU	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULPU	0331	MICROSCOPY ONLY STAINED PREP	38.41
CULSP	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULTI	0331	MICROSCOPY ONLY STAINED PREP	36.93
CULTI	0331	MICROSCOPY ONLY STAINED PREP	38.41
CULCT	0162	RAPID AUTOMATED ANTIBIOTIC SUSCEPTIBILIT	133.11
CULPU	0162	RAPID AUTOMATED ANTIBIOTIC SUSCEPTIBILIT	127.99
CULTI	0162	RAPID AUTOMATED ANTIBIOTIC SUSCEPTIBILIT	127.99
CULCT	0161	RAPID AUTOMATED BACTERIAL IDENTIFICATION	117.34
CULPU	0161	RAPID AUTOMATED BACTERIAL IDENTIFICATION	112.83
CULTI	0161	RAPID AUTOMATED BACTERIAL IDENTIFICATION	112.83
CULUR	0425	URINE BACTERIAL INHIBITION	28.58
CULUR	0415	URINE CULTURE IDENTIFICATION	47.44
CULUR	0405	URINE MICROSCOPY	36.93

8.5.3 Xpert MRSA Costing Information

Table 33: Price of Cepheid Xpert MRSA Kits from the Quote Requested and Received (QT1005SP)

Description	Unit Price (R)	VAT 14 %	Total Price (R)	Price per Test (R)
Xpert MRSA/SA, SSTI	2697.50	377.65	3075.15	307.52
Xpert MRSA/SA,BC	2697.50	377.65	3075.15	307.52
Xpert SA Nasal Complete 10 Test Kits	2697.50	377.65	3075.15	307.52

APPENDIX 6

8.6 Codes and Categories Identified from the Ethnographic Observations

8.6.1 Codes and Categories Identified from the Ethnographic Observations in the Clinical Wards

Table 34: Detailed Codes and Categories Identified from the Ethnographic Observations in the Clinical Wards

Categories / Codes	Communication	Routine	Patient Records	Infection Control	Antibiotics	Inconsistent	Specimen For MCS	Delay	Infection
HCP-HCP	X								
HCP-Patient	X			X					
HCPs	X					X			
Ward Rounds	X	X	X	X					
Nurses	X	X		X					
Doctors' notes			X			X			
Prescriptions			X					X	
X-rays			X						
NHLS reports			X		X		X	X	X
Antiseptic hand rub				X		X			
Hand-washing				X		X			
PPE				X		X			
Protocols						X			
Empiric					X			X	X
Changed					X			X	
Authorisation					X			X	
Redone							X		
Wound Irrigation							X		
Pre/Post-op					X		X		X
Isolation				X				X	X
Confirmed							X		X
Suspected							X		X

8.6.2 Codes and Categories Identified from the Ethnographic Observations in the NHLS Microbiology Laboratory

Table 35: Detailed Codes and Categories Identified from the Ethnographic Observations in the NHLS Microbiology Laboratory

Categories / Codes	Suspected MRSA Infection	Conventional Culture Method	Hands-on Time	Incubation Time	Results	Disposable Resources	Fixed Resources
Specimen	X						
Gram-positive cocci in clusters	X						
Catalase positive	X						
Staphylococcus	X						
Staphaurex-positive	X						
Staphylococcus aureus	X						
FOX Zone	X						
Vanco Etest	X						
Planting		X					
Microscopy		X					
Culture		X					
Picking		X					
Sensitivity		X					
Vanco Etest		X					
Ten minutes			X				
Five minutes			X				
Five to ten minutes			X				
24 Hours				X			
48 Hours				X			
72 Hours				X			
Recorded					X		
Working card					X		
Computer system					X		
Provisional					X		
Checked					X		
Finalised					X		
Agar plates						X	

Swab						X	
Microscopy slide						X	
Stains						X	
Water						X	
Immersion oil						X	
Catalase test kit						X	
Staphaurex test kit						X	
Saline						X	
Antibiotic discs						X	
Etest strip						X	
Microscope							X
Hot-plate							X
Metal rods							X
Inoculation loops							X
Test tubes							X
Bunsen-burner							X
Incubator							X
Antibiotic disc dispensers							X

8.6.3 Codes and Categories Identified from the Ethnographic Observations in the Antibiotic Dispensary

Table 36: Detailed Codes and Categories Identified from the Ethnographic Observations in the Antibiotic Dispensary

Categories / Codes	Protocols	Prescribing	Dispensing	Nurses	Urgent	Authorisation	Antibiotic Stewardship	Problems
Not written	X							
Differ	X							
Per-patient	X	X	X			X		
Ward	X	X	X				X	
Doctors		X				X	X	
Patient's prescription chart		X						
Dispensary order form		X		X				
Motivation		X				X		
Runners			X					
Dispensary	X		X				X	
Waiting			X			X		X
Three/five/seven days			X					
Manage ward stock				X				
Administer				X				
Emergency cupboard				X	X			
On-call					X			
Roll-over				X	X			
Restricted						X		
Vancomycin						X		
Linezolid						X		
Carbapenems						X		
MCS results						X		
Pharmacist inactive							X	
Advantages							X	
Out of stock							X	X
Expired							X	X
Communication							X	X

8.7 Cost Calculations

8.7.1 Antibiotic Cost Calculations

Table 37: The Daily Cost and Total Utilization Cost for Each Antibiotic Administered to Each Patient in the Orthopaedic Ward in 2013

Patient Number	Antibiotic and Dose	Utilization Cost (R)	
		Daily	Total
369P03	Augmentin PO 625 mg TDS for 14 days	3.47	48.52
	Gentamicin Irrigation system 80 mg x 20 drops 4 hourly for 10 days	95.76	957.60
	Rifampicin PO 600 mg daily for 4 days	0.85	3.39
	Vancomycin Irrigation System 1 g X 20 drops 4 hourly for 5 days	281.81	1409.04
369P09	Cloxacillin Irrigation System 1 g X 20 drops 4 hourly for 2 doses	20.98	20.98
	Gentamicin Irrigation System 80 mg x 20 drops 4 hourly for 10 days	95.76	957.60
369P12	Vancomycin 9 g stat for 9 days	422.71	3804.41
	Cefotaxime 9 g stat for 9 days	184.68	1662.12
	Cloxacillin IVI 1 g QID for 10 days	41.95	419.52
	Kefzol IVI 2 g in op	8.00	8.00
	Gentamicin Irrigation System 80 mg X 20 drops 4 hourly for 3 days	95.76	287.28
	Vancomycin Irrigation System 1 g X 20 drops 4 hourly for 8 days	281.81	2254.46
	Rifampicin PO 600 mg BD for 6 days	1.70	10.18
	Linezolid PO 600 mg BD for 6 days	564.49	3386.94
	Vancomycin IVI 1 g BD for 1 day	93.94	93.94
369P15	Kefzol IVI 1 g TDS for 12 days	12.00	144.05
	Kefzol 1 g In op	4.00	4.00
	Kefzol 2 g In op	8.00	8.00
	Kefzol 2 g In op	8.00	8.00
	Kefzol 1 g In op	4.00	4.00
	Kefzol 1 g stat in op	4.00	4.00
	Cloxacillin PO 1 g QID for 15 days	15.28	229.18
	Vancomycin IVI 1 g BD 9 days	93.94	845.42
369P06	Augmentin PO 625 mg TDS for 29 days	3.47	100.51
	Gentamicin Irrigation System 80 mg X 20 drops X 4 hourly for 32 days	95.76	3064.32
	Ertapenem IVI 250 mg QID for 1 day	368.33	368.33
	Rifampicin PO 600 mg BD for 17 days	1.70	28.84
	Vancomycin IVI 1 g daily for 6 days	46.97	281.81
	Kefzol 2 g In op	8.00	8.00
369P08	Gentamicin Irrigation System 80 mg x 20 drops 4 hours for 22 days	95.76	2106.72
	Kefzol IVI 1 g 3 doses TDS in op for 1 day	12.00	12.00
	Augmentin PO 1 g BD for 13 days	2.71	35.20
	Rifampicin PO 600 mg BD for 14 days	1.70	23.75
	Vancomycin IVI 1 g BD for 14 days	93.94	1315.10
	Vancomycin Irrigation System 1 g 20 drops 4 hourly for 3 days	281.81	845.42
369P13	Kefzol IVI 2 g TDS in op	24.01	24.01
	Cloxacillin IVI 1 g QID for 6 days	41.95	251.71
	Cloxacillin IVI 1 g TDS for 1 day	31.46	31.46
369P14	Augmentin IVI 1.2 g TDS for 6 days	37.56	225.36
	Gentamicin Irrigation System 80 mg 20 drops 4 hourly for 11 days	95.76	1053.36
	Augmentin PO 1 g BD for 1 day	2.71	2.71
	Augmentin IVI 1.2 g TDS for 4 days	37.56	150.24

369P02	Kefzol IVI 1 g in op	4.00	4.00
	Ertapenem IVI 1 g daily for 6 days	368.33	2209.98
	Kefzol IVI 1 g 3 doses TDS for 1 day	12.00	12.00
	Flagyl PO 400 mg TDS for 7 days	0.41	2.85
369P04	Augmentin PO 625 mg TDS for 19 days	3.47	65.85
	Cloxacillin PO 1 g QID for 18 days	15.28	275.01
	Vancomycin IVI 1 g BD for 9 days	93.94	845.42
	Rifampicin PO 600 mg BD for 9 days	1.70	15.27
369P16	Kefzol 1 g TDS in op for 1 day	12.00	12.00
	Cloxacillin PO 1 g QID for 10 days	15.28	152.78
	Cloxacillin PO 1 g QID for 20 days	15.28	305.57
369P05	Ciprobay PO 500 mg BD for 32 days	0.92	29.37
	Kefzol IVI 2 g TDS for 5 days	24.01	120.04
	Gentamicin Irrigation System 80 mg 20 drops 4 hourly for 9 days	95.76	861.84
369P10	Augmentin IVI 0.6 g TDS for 3 days now start Cloxacillin	21.48	64.44
	Gentamicin Irrigation System 80 mg 20 drops 4 hourly for 14 days	95.76	1340.64
	Cloxacillin PO 1 g QID for 11 days	15.28	168.06
	Vancomycin IVI 1 g BD for 4 days	93.94	375.74
	Vancomycin Irrigation System 1 g 20 drops 4 hourly for 2 days	281.81	563.62
369P07	Gentamicin Irrigation System 80 mg 20 drops 4 hourly for 13 days	95.76	1244.88
	Kefzol IVI 1 g 3 doses TDS for 1 day	12.00	12.00
	Rifampicin PO 600 mg BD for 11 days	1.70	18.66
	Vancomycin IVI 1 g BD for 9 days	93.94	845.42
	Vancomycin Irrigation System 1 g 20 drops 4 hourly for 2 days	281.81	563.62
369P01	Gentamicin Irrigation System 80 mg 20 drops 4 hourly for 25 days	95.76	2394.00
	Vancomycin IVI 1 g BD for 19 days	93.94	1784.78
	Rifampicin PO 600 mg BD for 18 days	1.70	30.53
369P11	Kefzol IVI 1 g 3 Doses TDS for 1 day	12.00	12.00
	Gentamicin Irrigation System 80 mg 20 drops 4 hourly for 7 days	95.76	670.32
	Rifampicin PO 600 mg BD for 19 days	1.70	32.23
	Vancomycin IVI 1 g BD for 19 days	93.94	1784.78
	Ceftazidime IVI 2 g BD for 19 days	120.00	2279.93
	Vancomycin Irrigation System 1 g BD for 6 days	93.94	563.62
	Ceftazidime Irrigation System 1 g 20 drops for 1 day	32.74	32.74
	Vancomycin IVI 1 g in op	46.97	46.97
	Linezolid PO 600 mg BD for 1 day	564.49	564.49
Total		**6534.78**	**46804.99**

Table 38: The Daily Cost and Total Utilization Cost for Each Antibiotic Administered to Each Patient in the Vascular Ward in 2013

Patient Number	Antibiotic and Dose	Utilization Costs (R)	
		Daily	Total
395P02	Tazocin IVI 4.5 g QID for 2 days	240.00	480.00
	Ertapenem IVI 1 g BD for 4 days	736.66	2946.64
	Meropenem IVI 1 g TDS for 11 days	377.85	4156.35
	Tazocin IVI 4.5 g QID for 14 days	240.00	3360.00
	Clindamycin IVI 600 mg TDS for 17 days	31.46	534.89
	Vancomycin IVI 1 g Stat	46.97	46.968
	Vancomycin IVI 1 g BD for 11 days	93.94	1033.296
	Vancomycin IVI 1 g Stat	46.97	46.968
	Ciprofloxacin IVI 1 g QID for 4 days	621.80	2487.20
395P03	Augmentin IVI 1.2 g TDS for 6 days	37.56	225.36
	Flagyl IVI 500 mg TDS for 5 days	16.12	80.58
	Vancomycin IVI 500 mg BD for 5 days	46.97	234.84
	Ceftazidime IVI 1 g BD for 6 days	65.48	392.88
395P04	Meropenem IVI 1 g TDS for 4 days	377.85	1511.40
395P05	Augmentin IVI 1.2 g TDS for 5 days	37.56	187.80
	Meropenem IVI 500 mg TDS for 6 days	191.58	1149.48
	Cefepime IVI 1 g TDS for 9 days	61.38	552.42
	Meropenem IVI 1g BD for 9 days	251.90	2267.10
395P06	Augmentin IVI 1.2 g TDS for 1 day	37.56	37.56
	Cloxacillin IVI 1 g QID for 4 days	41.95	167.81
	Gentamicin 240 mg Daily for 3 days	47.88	143.64
	Augmentin IVI 1.2 g TDS for 1 day	37.56	37.56
	Tazocin IVI 4.5 g QID for 12 days	240.00	2880.00
	Imipenem IVI 1 g BD for 4 days	188.20	752.80
	Gentamicin IVI 240 mg daily for 3 days	47.88	143.64
	Imipenem IVI 1 g TDS for 5 days	282.30	1411.50
	Amoxil PO 1 g BD for 1 day	0.82	0.82
	Klacid PO 1 g BD for 1 day	7.68	7.68
	Imipenem IVI 1 g TDS for 1 day	282.30	282.30
	Amoxil PO 1 g BD for 13 days	0.82	10.61
	Klacid PO 1 g BD for 6 days	7.68	46.06
395P07	Flagyl IVI 500 mg TDS for 5 days	16.12	80.58
	Cefepime IVI 2 g TDS for 5 days	116.73	583.65
	Vancomycin IVI 2 g daily for 3 days	93.94	281.81
	Vancomycin IVI 2 g BD for 1 day	187.87	187.87
	Vancomycin IVI 500 mg Stat	23.48	23.484
	Vancomycin IVI 1 g BD for 3 days	93.94	281.81
395P08	Tazocin IVI 4.5 g QID for 5 days	240.00	1200.00
395P09	Tazocin IVI 4.5 mg QID for 2 days	240.00	480.00
	Meropenem IVI 1 g TDS for 11 days	377.85	4156.35
	Ciprobay IVI 400 mg BD for 12 days	124.36	1492.32
	Augmentin PO 625 mg TDS for 10 days	3.47	34.66
	Vancomycin IVI 1 g daily for 6 days	46.97	281.808
	Vancomycin IVI 1 g BD for 8 days	93.94	751.488
	Ertapenem IVI 1 g daily for 4 days	368.33	1473.32
395P11	Augmentin IVI 1.2 g TDS for 4 days	37.56	150.24

	Tazocin IVI 4.5 g QID for 6 days	240.00	1440.00
	Tazocin IVI 4.5 g QID for 1 day	240.00	240.00
395P12	Augmentin PO 1 g BD for 19 days	2.71	51.45
395P13	Augmentin IVI 1.2 g TDS for 6 days	37.56	225.36
	Ciprobay PO 500 mg BD for 9 days	0.92	8.26
395P14	Cefepime IVI 1 g BD for 2 days	40.92	81.84
	Meropenem IVI 500 mg TDS for 6 days	191.58	1149.48
395P16	Tazocin IVI 2.25 g QID for 2 days	120.00	240.00
	Tazocin IVI 2.25 g QID for 10 days	120.00	1200.00
	Ertapenem IVI 1 g BD (1 dose)	368.33	368.33
	Flagyl PO 400 mg TDS for 4 days	0.30	1.22
395P17	Augmentin IVI 1.2 g TDS for 6 days	37.56	225.36
395P18	Cloxacillin IVI 1 g QID for 13 days	41.95	545.38
	Augmentin PO 625 mg TDS for 12 days	3.47	41.59
	Augmentin IVI 1.2 g TDS for 6 days	37.56	225.36
	Vancomycin IVI 1 g BD for 9 days	93.94	845.42
395P19	Cloxacillin PO 2g QID for 3 days	30.56	91.67
	Vancomycin 500 mg TDS (1 dose)	23.48	23.48
	Ceftazidime IVI 1 g BD 9 days	65.48	589.32
395P20	Kefzol IVI 2 g Stat	8.00	8.00
395P21	Augmentin IVI 1.2 g TDS for 8 days	37.56	300.48
	Tazocin IVI 4.5 g QID for 13 days	240.00	3120.00
	Meropenem IVI 1 g stat	125.95	125.95
	Tazocin IVI 4.5 g QID for 1 day	240.00	240.00
	Flagyl IVI 500 mg TDS for 11 days	16.12	177.28
	Vancomycin IVI 1 g BD for 2 days	93.94	187.87
	Tazocin IVI 4.5 g QID for 7 days	240.00	1680.00
	Flagyl PO 400 mg TDS for 2 days	0.30	0.61
	Meropenem IVI 1 g TDS for 1 day	377.85	377.85
	Tazocin IVI 4.5 g Stat	60.00	60.00
395P22	Tazocin IVI 4.5 g QID for 3 days	240.00	720.00
	Gentamicin IVI 240 mg daily for 7 days	47.88	335.16
395P23	Tazocin IVI 4.5 g QID for 13 days	240.00	3120.00
	Tazocin IVI 4.5 g QID for 1 day	240.00	240.00
	Cefepime IVI 1 BD for 4 days	40.92	163.68
	Amikacin 750 mg Stat	20.61	20.61
395P24	Augmentin IVI 1.2 g TDS for 8 days	37.56	300.48
	Vancomycin IVI 1 g BD for 1 day	93.94	93.936
395P25	Augmentin IVI 1.2 g TDS for 1 day	37.56	37.56
	Tazocin IVI 4.5 g QID for 7 days	240.00	1680.00
	Ciprofloxacin IVI 400 mg TDS for 4 days	186.54	746.16
	Rifampicin IVI 600 mg daily for 3 days	314.42	943.26
	Vancomycin IVI 1 g daily for 2 days	46.97	93.94
	Ertapenem IVI 1 g BD for 1 day (1 dose)	368.33	368.33
	Vancomycin IVI 1 g BD for 1 day (1 dose)	46.97	46.968
395P28	Augmentin IVI 1.2 g TDS for 5 days	37.56	187.80

	Vancomycin IVI 1 g BD for 2 days	93.94	187.87
395P29	Flagyl IVI 500 mg TDS for 5 days	16.12	80.58
	Zinacef IVI 1.5 g TDS for 3 days	47.06	141.18
	Cefepime IVI 1 g BD for 7 days	40.92	286.44
395P30	Tazocin IVI 4.5 g QID 6 days	240.00	1440.00
	Tazocin IVI 4.5 g TDS for 11 days	180.00	1980.00
	Bactrim Oral 480 mg BD for 1 day	0.25	0.25
	Bactrim Oral 960 mg BD for 7 days	0.51	3.55
	Meropenem IVI 500 mg TDS for 5 days	191.58	957.90
395P31	Augmentin Oral 1 g TDS for 4 days	4.06	16.25
395P32	Augmentin IVI 1.2 g QID for 20 days	50.08	1001.60
395P33	Augmentin PO 625 mg TDS for 13 days	3.47	45.06
395P36	Augmentin IVI 1.2 g TDS for 13 days	37.56	488.28
	Vancomycin IVI 1 g TDS for 2 days	140.90	281.81
	Vancomycin IVI 1 g daily for 3 days	46.97	140.90
	Vancomycin IVI 1 g BD for 4 days	93.94	375.74
	Cefepime IVI 1 g BD for 2 days	40.92	81.84
Total		**13412.76**	**69554.23**

8.7.2 NHLS Laboratory Test Cost Calculation

Table 39: Cost of Each NHLS Laboratory Test that Isolated MRSA per Patient in the Orthopaedic Ward in 2013

Patient Number	Laboratory Test Number	Cost (R)		Total Price (R)
		Microscopy	Culture and Sensitivity	
369P03	LT601	36.93	291.22	328.15
	LT602	36.93	139.29	176.22
	LT603	36.93	139.29	176.22
	LT604	36.93	291.22	328.15
	LT605	36.93	291.22	328.15
	LT606	36.93	291.22	328.15
369P09	LT607	36.93	315.05	351.98
	LT608	36.93	223.2	260.13
369P12	LT609	36.93	291.22	328.15
	LT610	36.93	291.22	328.15
369P15	LT611	36.93	223.2	260.13
369P06	LT612	36.93	223.2	260.13
	LT613	36.93	351.4	388.33
369P08	LT614	36.93	419.21	456.14
	LT615	36.93	356.28	393.21
	LT616	36.93	356.28	393.21
	LT617	36.93	199.46	236.39
	LT618	36.93	322.27	359.20
	LT619	36.93	498.03	534.96
	LT620	36.93	555.87	592.80
369P13	LT621	36.93	223.2	260.13
369P14	LT622			
	LT623			
369P02	LT624	36.93	223.2	260.13
369P04	LT625	36.93	223.2	260.13
369P16	LT626	38.41	232.13	270.54
369P05	LT627	36.93	199.46	236.39
	LT628	36.93	532.04	568.97
369P10	LT629	36.93	223.2	260.13
	LT630	36.93	281.04	317.97
369P07	LT631	36.93	267.39	304.32
	LT632	36.93	351.39	388.32

369P01	LT633	36.93	291.22	328.15
	LT634	36.93	291.22	328.15
	LT635	36.93	291.22	328.15
	LT636	36.93	291.22	328.15
	LT637	36.93	291.22	328.15
	LT638	36.93	291.22	328.15
	LT639	36.93	223.2	260.13
	LT640	36.93	471.74	508.67
	LT641	36.93	81.45	118.38
	LT642	36.93	291.22	328.15
369P11	LT643	36.93	555.87	592.80
	LT644	36.93	315.05	351.98
	LT645	36.93	291.22	328.15
	LT646	36.93	315.05	351.98
Total		**1626.40**	**13117.72**	**14744.12**

Table 40: Cost of Each NHLS Laboratory Test that Isolated MRSA per Patient in the Vascular Ward in 2013

Patient Number	Laboratory Test Number	Cost (R)		Total Price (R)
		Microscopy	Culture and Sensitivity	
395P02	LT501	36.93	599.94	636.87
	LT502	36.93	433.07	470.00
395P03	LT503	36.93	409.24	446.17
	LT504	36.93	223.2	260.13
395P04	LT505	36.93	223.2	260.13
395P05	LT506	36.93	532.04	568.97
395P06	LT507	36.93	223.2	260.13
	LT508	36.93	316.96	353.89
	LT509	36.93	247.03	283.96
395P07	LT510	38.41	267.5	305.91
	LT511	38.41	278.09	316.50
395P08	LT512	36.93	592.08	629.01
395P09	LT513	36.93	223.2	260.13
395P11	LT514	36.93	131.44	168.37
395P12	LT515	36.93	223.2	260.13
395P13	LT516	36.93	223.2	260.13
	LT517	36.93	223.2	260.13
395P14	LT518	36.93	317.39	354.32
	LT519	38.41	232.13	270.54
	LT520	38.41	498.79	537.20
	LT521	38.41	291.58	329.99
395P16	LT522	36.93	623.47	660.40
	LT523	36.93	280.37	317.30
369P17	LT524	38.41	341.84	380.25
395P18	LT525	36.93	223.2	260.13
	LT526	36.93	440.28	477.21
395P19	LT527	36.93	247.03	283.96
395P20	LT528	36.93	291.22	328.15
	LT529	36.93	315.05	351.98
395P21	LT530	36.93	341.22	378.15

	LT531	36.93	317.39	354.32
395P22	LT532	36.93	479.38	516.31
395P23	LT533	36.93	223.2	260.13
369P24	LT534	36.93	510.64	547.57
395P25	LT535	36.93	351.4	388.33
	LT536	36.93	288.26	325.19
395P28	LT537	36.93	223.2	260.13
395P29	LT538	38.41	232.13	270.54
395P30	LT539	36.93	356.27	393.20
	LT540	36.93	233.38	270.31
395P31	LT541	36.93	579.7	616.63
395P32	LT542	38.41	354.96	393.37
395P33	LT543			
395P36	LT544	36.93	291.22	328.15
	LT545	36.93	521.86	558.79
Total		**1636.76**	**14776.35**	**16413.11**

8.7.3 Antibiotic Utilization plus NHLS Laboratory Tests Cost Calculation

Table 41: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted that Isolated MRSA per Patient in the Orthopaedic Ward in 2013

Patient Number	Total Cost (R)		
	Antibiotic Utilization	Laboratory Test	Antibiotic Plus Laboratory Test
369P03	2418.56	1665.04	**4083.60**
369P09	978.58	612.11	**1590.69**
369P12	11926.85	656.30	**12583.15**
369P15	1246.66	260.13	**1506.79**
369P06	3851.81	648.46	**4500.27**
369P08	4338.20	2965.91	**7304.11**
369P13	307.18	260.13	**567.31**
369P14	1431.67	0.00	**1431.67**
369P02	2228.84	260.13	**2488.97**
369P04	1201.56	260.13	**1461.69**
369P16	470.36	270.54	**740.90**
369P05	1011.25	805.36	**1816.61**
369P10	2512.50	578.10	**3090.60**
369P07	2684.58	692.64	**3377.22**
369P01	4209.32	3184.23	**7393.55**
369P11	5987.08	1624.91	**7611.99**
Total	**46804.99**	**14744.12**	**61549.11**

Table 42: Total Cost of Antibiotics Administered plus NHLS Laboratory Tests Conducted that Isolated MRSA per Patient in the Vascular Ward in 2013

Patient Number	Total Cost (R)		
	Antibiotic Utilization	Laboratory Test	Antibiotic Plus Laboratory Test
395P02	15092.31	1106.87	**16199.18**
395P03	933.66	706.30	**1639.96**
395P04	1511.40	260.13	**1771.53**
395P05	4156.8	568.97	**4725.77**
395P06	5921.98	897.98	**6819.96**
395P07	1439.20	622.41	**2061.61**
395P08	1200.00	629.01	**1829.01**
395P09	8669.95	260.13	**8930.08**
395P11	1830.24	168.37	**1998.61**
395P12	51.45	260.13	**311.58**
395P13	233.62	520.26	**753.88**
395P14	1231.32	1492.05	**2723.37**
395P16	1809.55	977.70	**2787.25**
395P17	225.36	380.25	**605.61**
395P18	1657.75	737.34	**2395.09**
395P19	704.47	283.96	**988.43**
395P20	8.00	680.13	**688.13**
395P21	6270.04	732.47	**7002.51**
395P22	1055.16	516.31	**1571.47**
395P23	3544.29	260.13	**3804.42**
395P24	394.416	547.57	**941.99**

395P25	3916.214	713.52	**4629.73**
395P28	375.67	260.13	**635.80**
395P29	508.20	270.54	**778.74**
395P30	4381.70	663.51	**5045.21**
395P31	16.25	616.63	**632.88**
395P32	1001.6	393.37	**1394.97**
395P33	45.06	0.00	**45.06**
395P36	1368.58	886.94	**2255.52**
Total	**69554.23**	**16413.11**	**85967.34**

8.8 Decision-Tree-Analytic Models in Rollback

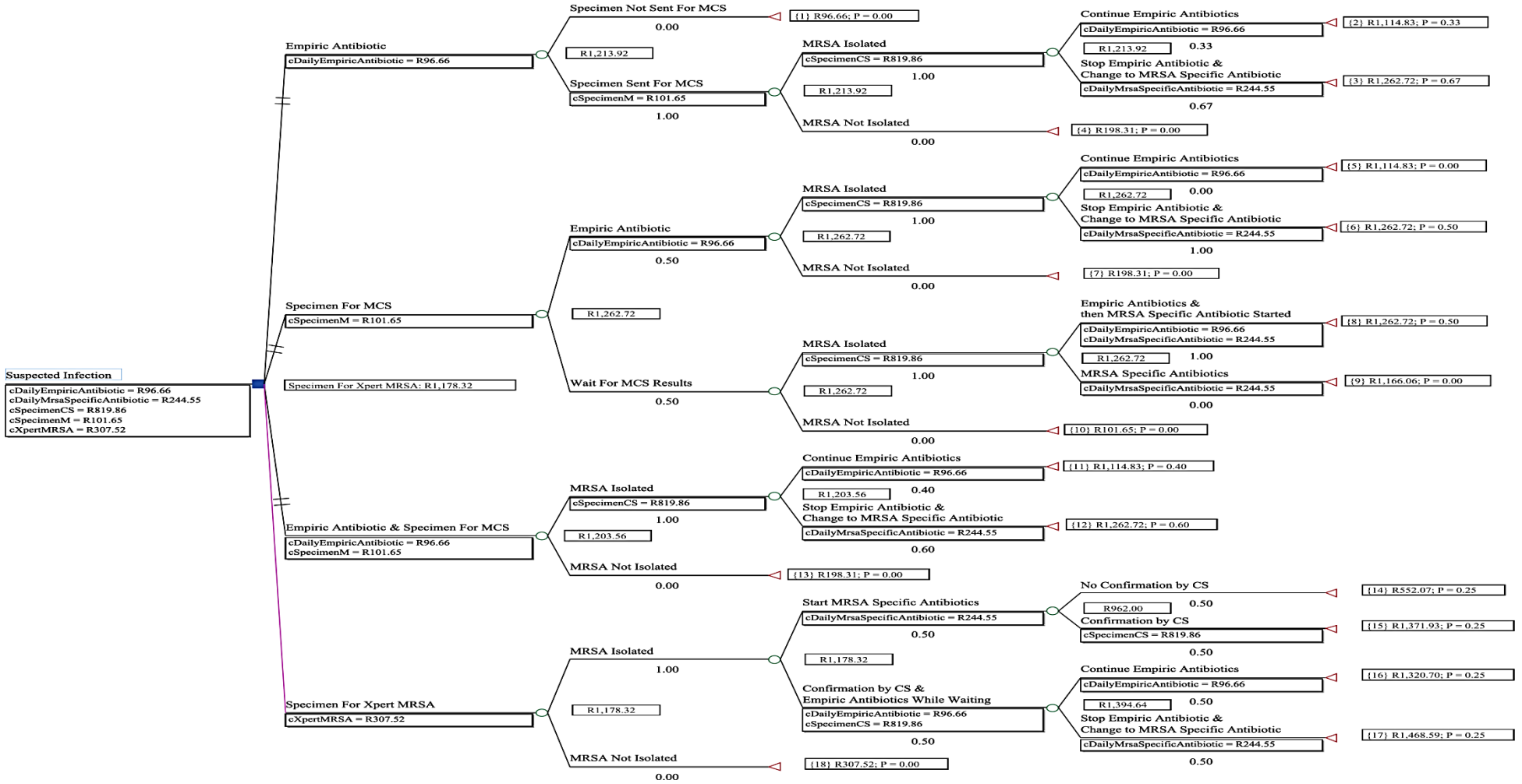


Figure 37: Rollback of Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward

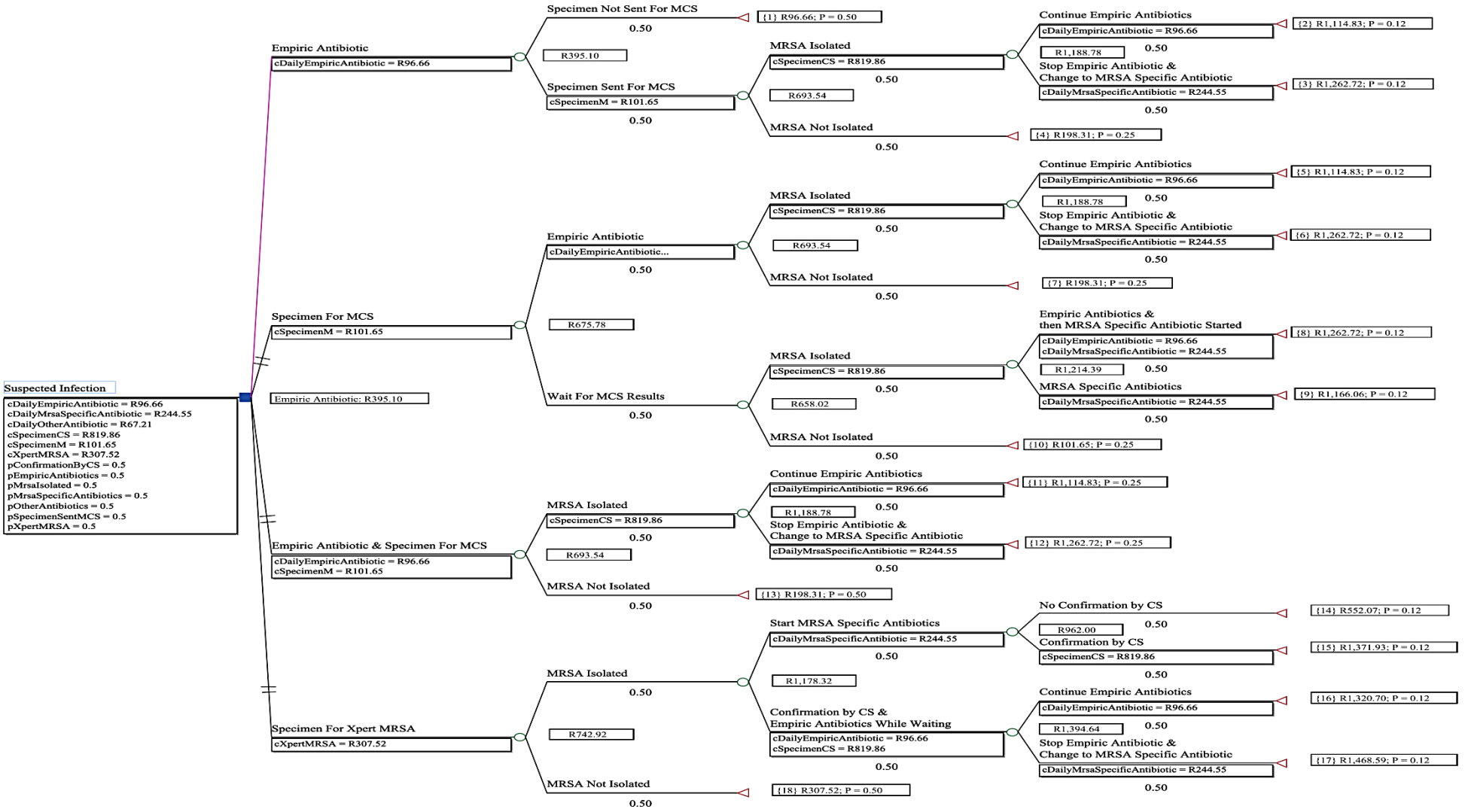


Figure 38: Rollback of Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Orthopaedic Ward

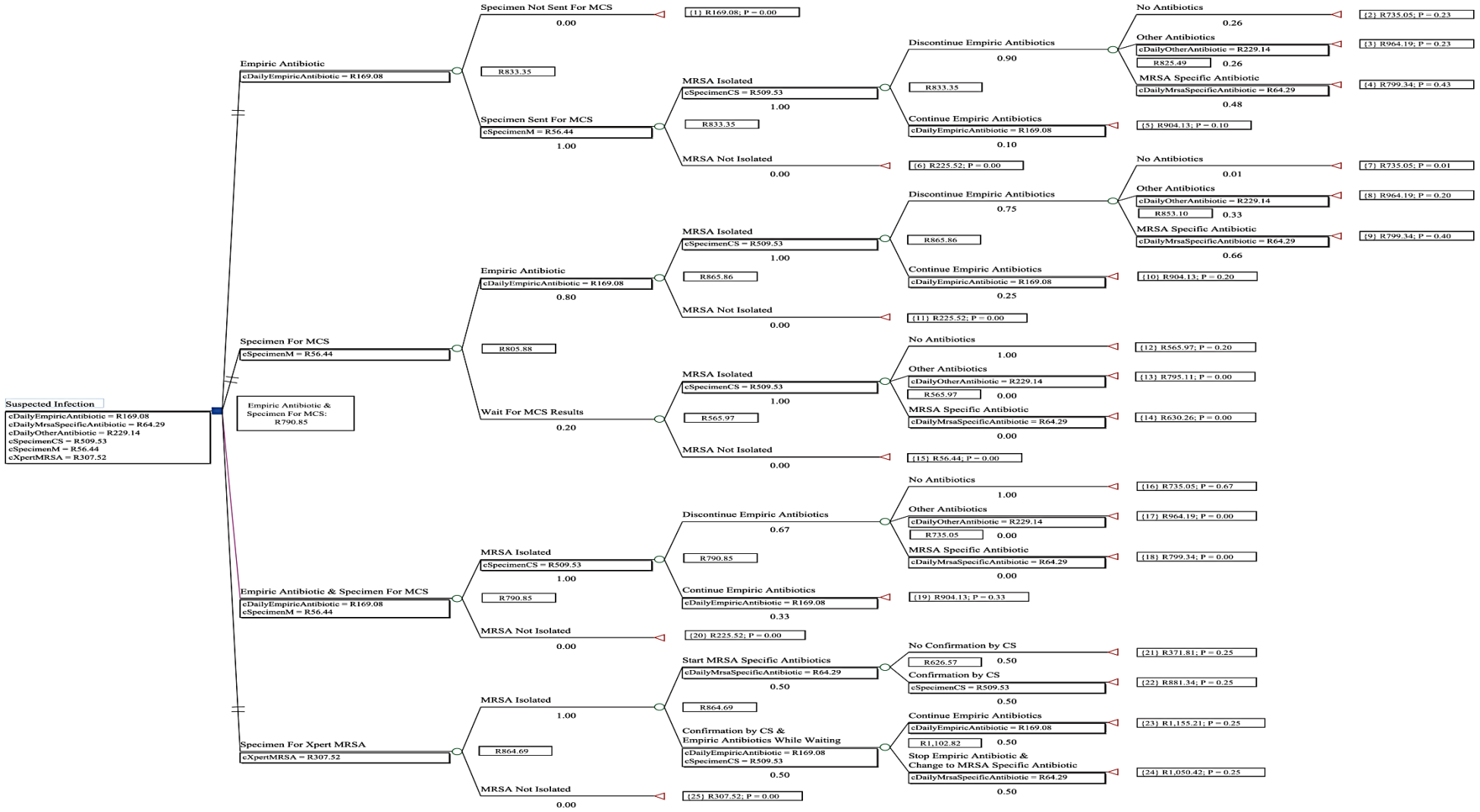


Figure 39: Rollback of Actual Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward

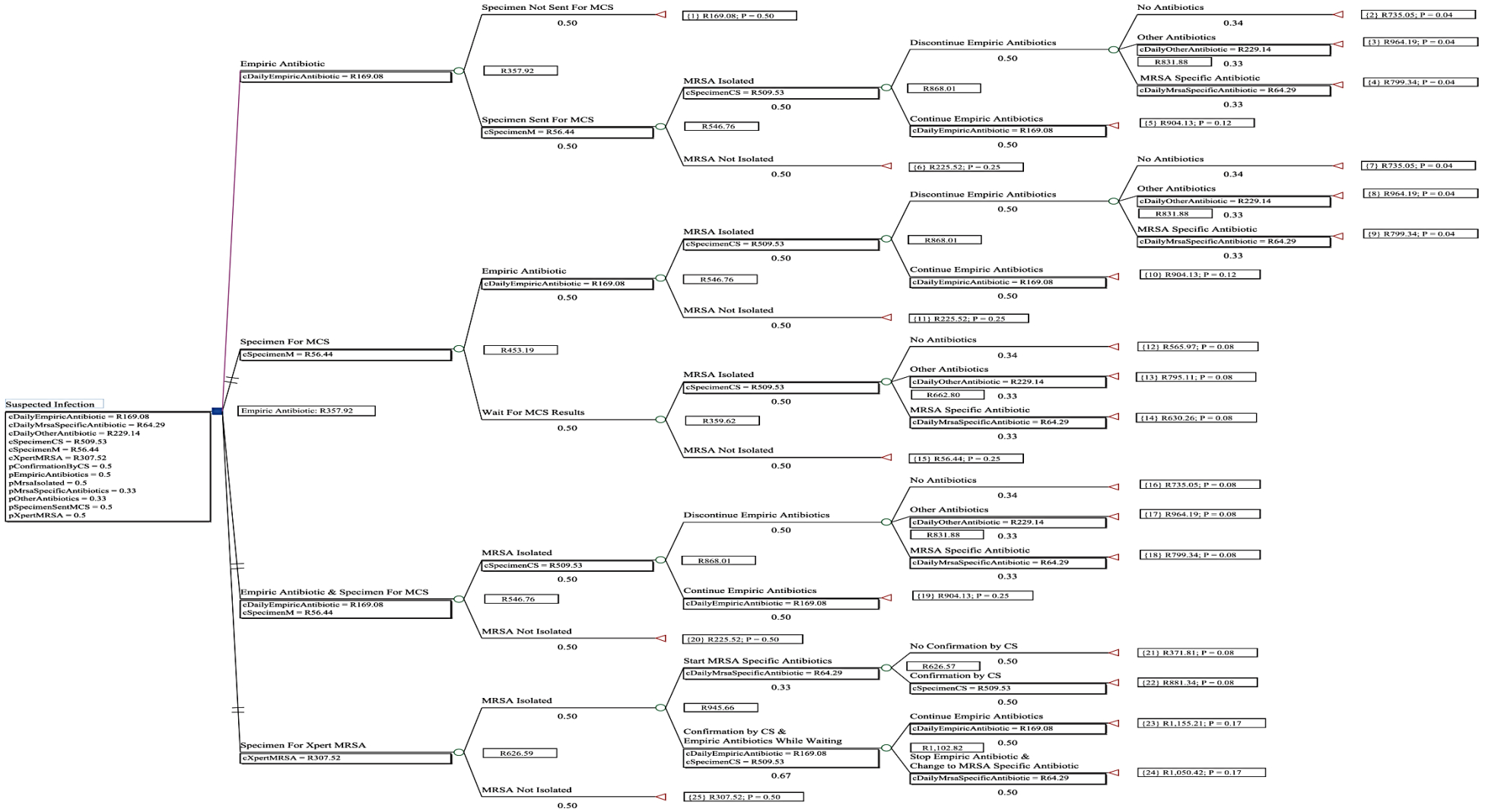


Figure 40: Rollback of Equal Decision-Tree-Analytic Model Showing the Management Pathways for a Patient with a Suspected Infection in the Vascular Ward

8.9 Threshold Analysis

Table 43: Threshold Analysis for the Actual Decision-Tree-Analytic Model in the Orthopaedic Ward

Variable	Variable Value (R)	Strategy 1	Strategy 2	Expected Value (R)
cSpecimenM	76.41	Empiric Antibiotic & Specimen For MCS	Specimen For Xpert MRSA	1178.32
cSpecimenCS	718.89	Empiric Antibiotic & Specimen For MCS	Specimen For Xpert MRSA	1102.60
cDailyMrsaSpecificAntibiotic	412.83	Specimen For Xpert MRSA	Empiric Antibiotic & Specimen For MCS	1304.53
cDailyEmpiricAntibiotic	57.83	Empiric Antibiotic & Specimen For MCS	Specimen For Xpert MRSA	1149.20
cXpertMRSA	332.76	Specimen For Xpert MRSA	Empiric Antibiotic & Specimen For MCS	1203.56

Table 44: Threshold Analysis for the Actual Decision-Tree-Analytic Model in the Vascular Ward

Variable	Variable Value (R)	Strategy 1	Strategy 2	Expected Value (R)
cDailyEmpiricAntibiotic	214.63	Empiric Antibiotic & Specimen For MCS	Specimen For MCS	851.43
cDailyMrsaSpecificAntibiotic	26.33	Specimen For MCS	Empiric Antibiotic & Specimen For MCS	790.85
cDailyOtherAntibiotic	153.22	Specimen For MCS	Empiric Antibiotic & Specimen For MCS	790.85
cXpertMRSA	233.67	Specimen For Xpert MRSA	Empiric Antibiotic & Specimen For MCS	790.85

Table 45: Threshold Analysis for the Equal Decision-Tree-Analytic Model in the Orthopaedic Ward

Variable	Variable Value (R)	Strategy 1	Strategy 2	Expected Value (R)
pSpecimenSentMCS	0.97	Empiric Antibiotic	Specimen For MCS	675.78

Table 46: Threshold Analysis for the Equal Decision-Tree-Analytic Model in the Vascular Ward

Variable	Variable Value (R)	Strategy 1	Strategy 2	Expected Value (R)
cDailyEmpiricAntibiotic	359.62	Empiric Antibiotic	Specimen For MCS	572.28
pMrsaIsolated	0.19	Specimen For MCS	Empiric Antibiotic	256.98
pSpecimenSentMCS	0.75	Empiric Antibiotic	Specimen For MCS	453.19

8.10 Plagiarism Report

SadiyyaAhmedHassenMScMedDissertation27102015.docx

ORIGINALITY REPORT

5%	4%	2%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	"Clinical Pharmacology", Basic & Clinical Pharmacology & Toxicology, 2014. Publication	<1%
2	www.ncbi.nlm.nih.gov Internet Source	<1%
3	wcp2014.org Internet Source	<1%
4	apps.who.int Internet Source	<1%
5	Bounthavong, Mark, and Donald I Hsu. "Cost–effectiveness of linezolid in methicillin-resistant *Staphylococcus aureus* skin and skin structure infections", Expert Review of Pharmacoeconomics & Outcomes Research, 2012. Publication	<1%
6	wiredspace.wits.ac.za Internet Source	<1%
7	Submitted to Cranfield University Student Paper	<1%
	"Research Podium Abstracts", Value in	

9. REFERENCES

Adaleti R, Nakipoglu Y, Karahan ZC, Tasdemir C, Kaya F (2008). Comparison of Polymerase Chain Reaction and Conventional Methods in Detecting Methicillin-Resistant Staphylococcus aureus. *J Infect Dev Ctries* **2**(1)**:** 46-50. doi: 10.3855/jidc.321

Andersen BM, Tollefsen T, Seljordslia B, Hochlin K, Syversen G, Jonassen TØ*, et al.* (2010). Rapid MRSA Test in Exposed Persons: Costs and Savings in Hospitals. *J Infect* **60**(4)**:** 293-299. doi: 10.1016/j.jinf.2010.01.008

Ataguba JE, Akazili J, McIntyre D (2011). Socioeconomic-Related Health Inequality in South Africa: Evidence from General Household Surveys. *Int J Equity Health* **10**(1)**:** 48. doi: 10.1186/1475-9276-10-48

Bamford C, Bonorchis K, Ryan A, Simpson J, Elliott E, Hoffmann R*, et al.* (2011). Antimicrobial Susceptibility Patterns of Selected Bacteraemic Isolates from South African Public Sector Hospitals, 2010. *South Afr J Epidemiol Infect* **26**(4)**:** 243-250

Bekker LG, Venter F, Cohen K, Goemare E, Van Cutsem G, Boulle A*, et al.* (2014). Provision of Antiretroviral Therapy in South Africa: The Nuts and Bolts. *Antivir Ther* **19**(Suppl 3)**:** 105-116. doi: 10.3851/IMP2905

Blaya JA, Fraser HS, Holt B (2010). E-Health Technologies Show Promise in Developing Countries. *Health Aff* **29**(2)**:** 244-251. doi: 10.1377/hlthaff.2009.0894

Bounthavong M, Hsu DI, Okamoto MP (2009). Cost-Effectiveness Analysis of Linezolid Vs. Vancomycin in Treating Methicillin-Resistant Staphylococcus aureus Complicated Skin and Soft Tissue Infections Using a Decision Analytic Model. *Int J Clin Pract* **63**(3)**:** 376-386. doi: 10.1111/j.1742-1241.2008.01958.x

Boyles TH, Wasserman S (2015). Diagnosis of Bacterial Infection. *S Afr Med J* **105**(5)**:** 419-419

Brenwald NP, Baker N, Oppenheim B (2010). Feasibility Study of a Real-Time PCR Test for Meticillin-Resistant Staphylococcus aureus in a Point of Care Setting. *J Hosp Infect* **74**(3)**:** 245-249. doi: 10.1016/j.jhin.2009.09.007

Brink A, Feldman C, Dusé A, Gopalan D, Grolman D, Mer M*, et al.* (2006). Guideline for the Management of Nosocomial Infections in South Africa. *South Afr J Epidemiol Infect* **21**(4)**:** 152-160

Brink A, Moolman J, da Silva MC, Botha M (2007). Antimicrobial Susceptibility Profile of Selected Bacteraemic Pathogens from Private Institutions in South Africa. *S Afr Med J* **97**(4)**:** 273-279

Brown J, Paladino JA (2010). Impact of Rapid Methicillin-Resistant Staphylococcus aureus Polymerase Chain Reaction Testing on Mortality and Cost Effectiveness in Hospitalized Patients with Bacteraemia: A Decision Model. *Pharmacoeconomics* **28**(7)**:** 567-575. doi: 10.2165/11533020-000000000-00000

Busby A, Gilchrist B (1992). The Role of the Nurse in the Medical Ward Round. *J Adv Nurs* **17**(3)**:** 339-346. doi: 10.1111/j.1365-2648.1992.tb01912.x

Calfee DP (2012). Crisis in Hospital-Acquired, Healthcare-Associated Infections. *Annu Rev Med* **63:** 359-371. doi: 10.1146/annurev-med-081210-144458

Centers for Disease Control and Prevention (2014). *Core Elements of Hospital Antibiotic Stewardship Programs*. Atlanta, GA: US Department of Health and Human Services.

Cepheid (2012). *Xpert ® MRSA/SA Blood Culture Assay: Package Insert*, 300-5441 Rev L edn. Sweden: Cepheid

Chopra M, Lawn JE, Sanders D, Barron P, Abdool Karim SS, Bradshaw D*, et al.* (2009). Achieving the Health Millennium Development Goals for South Africa: Challenges and Priorities. *Lancet* **374**(9694)**:** 1023-1031. doi: 10.1016/s0140-6736(09)61122-3

Coovadia H, Jewkes R, Barron P, Sanders D, McIntyre D (2009). The Health and Health System of South Africa: Historical Roots of Current Public Health Challenges. *Lancet* **374**(9692)**:** 817-834. doi: 10.1016/S0140-6736(09)60951-X

Cowie SE, Ma I, Lee SK, Smith RM, Hsiang YN (2005). Nosocomial MRSA Infection in Vascular Surgery Patients: Impact on Patient Outcome. *Vasc Endovascular Surg* **39**(4)**:** 327-334. doi: 10.1177/153857440503900404

Cunningham R, Jenks P, Northwood J, Wallis M, Ferguson S, Hunt S (2007). Effect on MRSA Transmission of Rapid PCR Testing of Patients Admitted to Critical Care. *J Hosp Infect* **65**(1)**:** 24-28. doi: 10.1016/j.jhin.2006.09.019

Dalton BR, Sabuda DM, Bresee LC, Conly JM (2015). Use of an Electronic Medication Administration Record (eMAR) for Surveillance of Medication Omissions: Results of a One Year Study of Antimicrobials in the Inpatient Setting. *PLoS One* **10**(4)**:** e0122422. doi: 10.1371/journal.pone.0122422

Datta P, Gulati N, Singla N, Rani Vasdeva H, Bala K, Chander J*, et al.* (2011). Evaluation of Various Methods for the Detection of Meticillin-Resistant Staphylococcus aureus Strains and Susceptibility Patterns. *J Med Microbiol* **60**(Pt 11)**:** 1613-1616. doi: 10.1099/jmm.0.032219-0

Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR (2004). Methicillin-Resistant Staphylococcus aureus (MRSA) Nares Colonization at Hospital Admission and Its Effect on Subsequent MRSA Infection. *Clin Infect Dis* **39**(6)**:** 776-782. doi: 10.1086/422997

Day C, Gray A (2015). Health and Related Indicators. In: Padarath A, King J, English R (eds). *South African Health Review*, 2014/2015 edn. Durban: Health Systems Trust. pp.295

De Wet L, McDonald T, Pistorius GJ (2001). The Electronic Patient Record (EPR) South Africa. *S Afr Fam Pract* **23**(5)**:** 5-11

de With K, Bestehorn H, Steib-Bauert M, Kern WV (2009). Comparison of Defined Versus Recommended Versus Prescribed Daily Doses for Measuring Hospital Antibiotic Consumption. *Infection* **37**(4)**:** 349-352. doi: 10.1007/s15010-008-8138-4

Department of Health (2007). *The National Infection Prevention and Control Policy & Strategy*. Pretoria, South Africa: National Department of Health.

Department of Health (2009). *Uniform Patient Fee Schedule for Paying Patients Attending Public Hospitals: User Guide - UPFS 2009*. Pretoria, South Africa: National Department of Health.

Department of Health (2012). *Standard Treatment Guidelines and Essential Drugs List for South Africa: Hospital Level Adults*. 3rd edn. Pretoria, South Africa: National Department of Health.

Department of Health (2013). *Guidelines for Pharmacoeconomic Submissions 2012*. Pretoria, South Africa: National Department of Health.

Department of Health (2014). *Antimicrobial Resistance National Strategy Framework, 2014-2024*. Pretoria, South Africa: National Department of Health.

Dhamend L (2011). Pharmacoeconomics and the Clinician: A South African Perspective. *S Afr Fam Pract* **53**(1)**:** 92-92. doi: 10.1080/20786204.2011.10874066

Dixon-Woods M, Suokas A, Pitchforth E, Tarrant C (2009). An Ethnographic Study of Classifying and Accounting for Risk at the Sharp End of Medical Wards. *Soc Sci Med* **69**(3)**:** 362-369. doi: 10.1016/j.socscimed.2009.05.025

Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL (2005). *Methods for the Economic Evaluation of Health Care Programmes*. 3rd edn. Oxford, United Kingdom: Oxford University Press. pp.7-17; 55-72; 247-308

Dusé AG (2005). Infection Control in Developing Countries with Particular Emphasis on South Africa. *South Afr J Epidemiol Infect* **20**(2)**:** 37-41

Dusé AG (2011). The Global Antibiotic Resistance Partnership (GARP). *S Afr Med J* **101**(8 Pt 2)**:** 551

Earnshaw JJ (2002). Methicillin-Resistant Staphylococcus aureus: Vascular Surgeons Should Fight Back. *Eur J Vasc Endovasc Surg* **24**(4)**:** 283-286. doi: 10.1053/ejvs.2002.1705

Edmond MB, Wenzel RP (2013). Screening Inpatients for MRSA – Case Closed. *N Engl J Med* **368**(24)**:** 2314-2315. doi: 10.1056/NEJMe1304831

Edwards B, Andini R, Esposito S, Grossi P, Lew D, Mazzei T*, et al.* (2014). Treatment Options for Methicillin-Resistant Staphylococcus aureus (MRSA) Infection: Where Are We Now? *J Glob Antimicrob Resist* **2**(3)**:** 133-140. doi: 10.1016/j.jgar.2014.03.009

Falagas ME, Karageorgopoulos DE, Leptidis J, Korbila IP (2013). MRSA in Africa: Filling the Global Map of Antimicrobial Resistance. *PLoS One* **8**(7)**:** e68024. doi: 10.1371/journal.pone.0068024

Fätkenheuer G, Hirschel B, Harbarth S (2014). Screening and Isolation to Control Meticillin-Resistant Staphylococcus aureus: Sense, Nonsense, and Evidence. *Lancet* **385**(9973)**:** 1146-1149. doi: 10.1016/S0140-6736(14)60660-7

Fortuin-de Smidt MC, Singh-Moodley A, Badat R, Quan V, Kularatne R, Nana T*, et al.* (2015). Staphylococcus aureus Bacteraemia in Gauteng Academic Hospitals, South Africa. *Int J Infect Dis* **30:** 41-48. doi: 10.1016/j.ijid.2014.10.011

Fraser HS, Biondich P, Moodley D, Choi S, Mamlin BW, Szolovits P (2005). Implementing Electronic Medical Record Systems in Developing Countries. *Inform Prim Care* **13**(2)**:** 83-95

French GL (2009). Methods for Screening for Methicillin-Resistant Staphylococcus aureus Carriage. *Clin Microbiol Infect* **15**(Suppl 7)**:** 10-16. doi: 10.10.1111/j.1469-0691.2009.03092.x

Gagliotti C, Ricchizzi E, Buttazzi R, Tumietto F, Resi D, Moro M (2014). Hospital Statistics for Antibiotics: Defined Versus Prescribed Daily Dose. *Infection* **42**(5)**:** 869-873. doi: 10.1007/s15010-014-0649-6

Gavaza P, Rascati KL, Oladapo AO, Khoza S (2012). The State of Health Economic Research in South Africa: A Systematic Review. *Pharmacoeconomics* **30**(10)**:** 925-940. doi: 10.2165/11589450-000000000-00000

Geiger K, Brown J (2013). Rapid Testing for Methicillin-Resistant Staphylococcus aureus: Implications for Antimicrobial Stewardship. *Am J Health Syst Pharm* **70**(4)**:** 335-342. doi: 10.2146/ajhp110724

Georgiou A, Prgomet M, Toouli G, Callen J, Westbrook J (2011). What Do Physicians Tell Laboratories When Requesting Tests? A Multi-Method Examination of Information Supplied to the Microbiology Laboratory before and after the Introduction of Electronic Ordering. *Int J Med Inform* **80**(9)**:** 646-654. doi: 10.1016/j.ijmedinf.2011.06.003

Girou E, Pujade G, Legrand P, Cizeau F, Brun-Buisson C (1998). Selective Screening of Carriers for Control of Methicillin-Resistant Staphylococcus aureus (MRSA) in High-Risk Hospital Areas with a High Level of Endemic MRSA. *Clin Infect Dis* **27**(3)**:** 543-550. doi: 10.1086/514695

Glance LG, Stone PW, Mukamel DB, Dick AW (2011). Increases in Mortality, Length of Stay, and Cost Associated with Hospital-Acquired Infections in Trauma Patients. *Arch Surg* **146**(7)**:** 794-801. doi: 10.1001/archsurg.2011.41

Glick SB, Samson DJ, Huang ES, Vats V, Aronson N, Weber SG (2014). Screening for Methicillin-Resistant Staphylococcus aureus: A Comparative Effectiveness Review. *Am J Infect Control* **42**(2)**:** 148-155. doi: 10.1016/j.ajic.2013.07.020

Goodson L, Vassar M (2011). An Overview of Ethnography in Healthcare and Medical Education Research. *J Educ Eval Health Prof* **8:** 4. doi: 10.3352/jeehp.2011.8.4

Gopalan P (2005). An Approach to the Patient Suspected of Having a Hospital-Acquired Infection. *South Afr J Epidemiol Infect* **20**(2)**:** 46-48

Gorwitz RJ, Kruszon-Moran D, McAllister SK, McQuillan G, McDougal LK, Fosheim GE*, et al.* (2008). Changes in the Prevalence of Nasal Colonization with Staphylococcus aureus in the United States, 2001-2004. *J Infect Dis* **197**(9)**:** 1226-1234. doi: 10.1086/533494

Gould IM (2006). Costs of Hospital-Acquired Methicillin-Resistant Staphylococcus aureus (MRSA) and Its Control. *Int J Antimicrob Agents* **28**(5)**:** 379-384. doi: 10.1016/j.ijantimicag.2006.09.001

Gow J, Strauss M, Whiteside A (2013). The State of Health Economic Research in South Africa. *Pharmacoeconomics* **31**(3)**:** 251-253. doi: 10.1007/s40273-013-0024-y

Graves N, Weinhold D, Tong E, Birrell F, Doidge S, Ramritu P*, et al.* (2007). Effect of Healthcare-Acquired Infection on Length of Hospital Stay and Cost. *Infect Control Hosp Epidemiol* **28**(3)**:** 280-292

Gray A (2014). Medicines Shortages-Unpicking the Evidence from a Year in South Africa. *Australas Med J* **7**(5)**:** 208-212. doi: 10.4066/amj.2014.1932

Ha JF, Longnecker N (2010). Doctor-Patient Communication: A Review. *Ochsner J* **10**(1)**:** 38-43

Halcomb EJ, Griffiths R, Fernandez R (2008). The Role of Patient Isolation and Compliance with Isolation Practices in the Control of Nosocomial MRSA in Acute Care. *Int J Evid Based Healthc* **6**(2)**:** 206-224. doi: 10.1111/j.1744-1609.2008.00089.x

Harbarth S, Hawkey PM, Tenover F, Stefani S, Pantosti A, Struelens MJ (2011). Update on Screening and Clinical Diagnosis of Meticillin-Resistant Staphylococcus aureus (MRSA). *Int J Antimicrob Agents* **37**(2)**:** 110-117. doi: 10.1016/j.ijantimicag.2010.10.022

Havill NL (2010). Recent Advances in MRSA Surveillance Detection. *Infectious Disease Special Edition* **13**(September 2010)**:** 31-35

Huang SS, Yokoe DS, Hinrichsen VL, Spurchise LS, Datta R, Miroshnik I*, et al.* (2006). Impact of Routine Intensive Care Unit Surveillance Cultures and Resultant Barrier Precautions on Hospital-Wide Methicillin-Resistant Staphylococcus aureus Bacteremia. *Clin Infect Dis* **43**(8)**:** 971-978. doi: 10.1086/507636

Hübner C, Hübner NO, Kramer A, Fleßa S (2012). Cost-Analysis of PCR-Guided Pre-Emptive Antibiotic Treatment of Staphylococcus aureus Infections: An Analytic Decision Model. *Eur J Clin Microbiol Infect Dis* **31**(11)**:** 3065-3072. doi: 10.1007/s10096-012-1666-y

Huletsky A, Giroux R, Rossbach V, Gagnon M, Vaillancourt M, Bernier M*, et al.* (2004). New Real-Time PCR Assay for Rapid Detection of Methicillin-Resistant Staphylococcus aureus Directly from Specimens Containing a Mixture of Staphylococci. *J Clin Microbiol* **42**(5)**:** 1875-1884. doi: 10.1128/jcm.42.5.1875-1884.2004

Huletsky A, Lebel P, Picard FJ, Bernier M, Gagnon M, Boucher N*, et al.* (2005). Identification of Methicillin-Resistant Staphylococcus aureus Carriage in Less Than 1 Hour During a Hospital Surveillance Program. *Clin Infect Dis* **40**(7)**:** 976-981. doi: 10.1086/428579

Iedema R, Hor S-Y, Wyer M, Gilbert GL, Jorm C, Hooker C*, et al.* (2015). An Innovative Approach to Strengthening Health Professionals' Infection Control and Limiting Hospital-Acquired Infection: Video-Reflexive Ethnography. *BMJ Innov* **0:** 1-6. doi: 10.1136/bmjinnov-2014-000032

Jansen van Rensburg MJ, Whitelaw AC, Elisha BG (2012). Genetic Basis of Rifampicin Resistance in Methicillin-Resistant Staphylococcus aureus Suggests Clonal Expansion in Hospitals in Cape Town, South Africa. *BMC Microbiol* **12:** 46. doi: 10.1186/1471-2180-12-46

Kelly KN, Monson JRT (2012). Hospital-Acquired Infections. *Surgery* **30**(12)**:** 640-644. doi: 10.1016/j.mpsur.2012.10.005

Kluytmans J (2007). Control of Meticillin-Resistant Staphylococcus aureus (MRSA) and the Value of Rapid Tests. *J Hosp Infect* **65**(Suppl 2)**:** 100-104. doi: 10.1016/s0195-6701(07)60024-3

Kluytmans J, Struelens M (2009). Meticillin Resistant Staphylococcus aureus in the Hospital. *BMJ* **338:** b364. doi: 10.1136/bmj.b364

Kupfer M, Jatzwauk L, Monecke S, Möbius J, Weusten A (2010). MRSA in a Large German University Hospital: Male Gender Is a Significant Risk Factor for MRSA Acquisition. *GMS Krankenhhyg Interdiszip* **5**(2)**:** Doc11. doi: 10.3205/dgkh000154

Lee BY, Tsui BY, Bailey RR, Smith KJ, Muder RR, Lewis GJ*, et al.* (2009). Should Vascular Surgery Patients Be Screened Preoperatively for Methicillin-Resistant Staphylococcus aureus? *Infect Control Hosp Epidemiol* **30**(12)**:** 1158-1165. doi: 10.1086/648087

Lee BY, Wiringa AE, Bailey RR, Goyal V, Tsui B, Lewis GJ*, et al.* (2010). The Economic Effect of Screening Orthopedic Surgery Patients Preoperatively for Methicillin-Resistant Staphylococcus aureus. *Infect Control Hosp Epidemiol* **31**(11)**:** 1130-1138. doi: 10.1086/656591

Li J, Ulvin K, Biboh H, Kristiansen IS (2012). Cost-Effectiveness of Supplementing a Broth-Enriched Culture Test with the Xpert Meticillin-Resistant Staphylococcus aureus (MRSA) Assay for Screening Inpatients at High Risk of MRSA. *J Hosp Infect* **82**(4)**:** 227-233. doi: 10.1016/j.jhin.2012.08.009

Liu W, Manias E, Gerdtz M (2013). Medication Communication During Ward Rounds on Medical Wards: Power Relations and Spatial Practices. *Health (London)* **17**(2)**:** 113-134. doi: 10.1177/1363459312447257

Machado AR, Arns CdC, Follador W, Guerra A (2005). Cost-Effectiveness of Linezolid Versus Vancomycin in Mechanical Ventilation-Associated Nosocomial Pneumonia Caused by Methicillin-Resistant Staphylococcus aureus. *Braz J Infect Dis* **9**(3)**:** 191-200. doi: 10.1590/s1413-86702005000300001

Malhotra-Kumar S, Abrahantes JC, Sabiiti W, Lammens C, Vercauteren G, Ieven M*, et al.* (2010). Evaluation of Chromogenic Media for Detection of Methicillin-Resistant Staphylococcus aureus. *J Clin Microbiol* **48**(4)**:** 1040-1046. doi: 10.1128/JCM.01745-09

Marimuthu K, Pittet D, Harbarth S (2014). The Effect of Improved Hand Hygiene on Nosocomial MRSA Control. *Antimicrob Resist Infect Control* **3:** 34. doi: 10.1186/2047-2994-3-34

Marlowe EM, Bankowski MJ (2011). Conventional and Molecular Methods for the Detection of Methicillin-Resistant Staphylococcus aureus. *J Clin Microbiol* **49**(9 Suppl)**:** S53-S56. doi: 10.1128/JCM.00791-11

Mayosi BM, Benatar SR (2014). Health and Health Care in South Africa--20 Years after Mandela. *N Engl J Med* **371**(14)**:** 1344-1353. doi: 10.1056/NEJMsr1405012

McGee S (2010). Pharmacoeconomics and Outcomes Research-What Is It and How Is It Being Applied in the South African Health Care System? *S Afr Pharm J* **77**(5)**:** 62-63

McGinigle KL, Gourlay ML, Buchanan IB (2008). The Use of Active Surveillance Cultures in Adult Intensive Care Units to Reduce Methicillin-Resistant Staphylococcus aureus-Related Morbidity, Mortality, and Costs: A Systematic Review. *Clin Infect Dis* **46**(11)**:** 1717-1725. doi: 10.1086/587901

McMillan J, Schumacher S (2014). *Research in Education: Evidence-Based Inquiry* 7th edn. Harlow: Pearson. pp.369-408

Mendelson M (2015). Role of Antibiotic Stewardship in Extending the Age of Modern Medicine. *S Afr Med J* **105**(5)**:** 414-418. doi: 10.7196/samj.9635

Mendelson M, Matsoso MP (2015). The South African Antimicrobial Resistance Strategy Framework. *AMR CONTROL* **2015**(1)**:** 54-61

Micek ST (2007). Alternatives to Vancomycin for the Treatment of Methicillin-Resistant Staphylococcus aureus Infections. *Clin Infect Dis* **45**(Suppl 3)**:** S184-190. doi: 10.1086/519471

Moody J, Septimus E, Hickok J, Huang SS, Platt R, Gombosev A*, et al.* (2013). Infection Prevention Practices in Adult Intensive Care Units in a Large Community Hospital System after Implementing Strategies to Reduce Health Care-Associated, Methicillin-Resistant Staphylococcus aureus Infections. *Am J Infect Control* **41**(2)**:** 126-130. doi: 10.1016/j.ajic.2012.02.017

Muller A, Monnet DL, Talon D, Hénon T, Bertrand X (2006). Discrepancies between Prescribed Daily Doses and WHO Defined Daily Doses of Antibacterials at a University Hospital. *Br J Clin Pharmacol* **61**(5)**:** 585-591. doi: 10.1111/j.1365-2125.2006.02605.x

Muto CA, Jernigan JA, Ostrowsky BE, Richet HM, Jarvis WR, Boyce JM*, et al.* (2003). SHEA Guideline for Preventing Nosocomial Transmission of Multidrug-Resistant Strains of Staphylococcus aureus and Enterococcus. *Infect Control Hosp Epidemiol* **24**(5)**:** 362-386. doi: 10.1086/502213

Naimi TS, LeDell KH, Como-Sabetti K, Borchardt SM, Boxrud DJ, Etienne J*, et al.* (2003). Comparison of Community- and Health Care-Associated Methicillin-Resistant Staphylococcus aureus Infection. *JAMA* **290**(22)**:** 2976-2984. doi: 10.1001/jama.290.22.2976

Nelson RE, Samore MH, Smith KJ, Harbarth S, Rubin MA (2010). Cost-Effectiveness of Adding Decolonization to a Surveillance Strategy of Screening and Isolation for Methicillin-Resistant Staphylococcus aureus Carriers. *Clin Microbiol Infect* **16**(12)**:** 1740-1746. doi: 10.1111/j.1469-0691.2010.03324.x

Nonhoff C, Denis O, Brenner A, Buidin P, Legros N, Thiroux C*, et al.* (2009). Comparison of Three Chromogenic Media and Enrichment Broth Media for the Detection of Methicillin-Resistant Staphylococcus aureus from Mucocutaneous Screening Specimens : Comparison of MRSA Chromogenic Media. *Eur J Clin Microbiol Infect Dis* **28**(4)**:** 363-369. doi: 10.1007/s10096-008-0637-9

Nyasulu P, Murray J, Perovic O, Koornhof H (2012). Antimicrobial Resistance Surveillance among Nosocomial Pathogens in South Africa: Systematic Review of Published Literature. *J Exp Clin Med* **4**(1)**:** 8-13. doi: 10.1016/j.jecm.2011.11.002

O'Grady NP, Barie PS, Bartlett JG, Bleck T, Carroll K, Kalil AC*, et al.* (2008). Guidelines for Evaluation of New Fever in Critically Ill Adult Patients: 2008 Update from the American College of Critical Care Medicine and the Infectious Diseases Society of America. *Crit Care Med* **36**(4)**:** 1330-1349. doi: 10.1097/CCM.0b013e318169eda9

Oostenbrink JB, Koopmanschap MA, Rutten FF (2002). Standardisation of Costs: The Dutch Manual for Costing in Economic Evaluations. *Pharmacoeconomics* **20**(7)**:** 443-454

Parcell B, Phillips G (2014). Use of Xpert® MRSA PCR Point-of-Care Testing Beyond the Laboratory. *J Hosp Infect* **87**(2)**:** 119-121. doi: 10.1016/j.jhin.2014.04.002

Paruk F, Richards G, Scribante J, Bhagwanjee S, Mer M, Perrie H (2012). Antibiotic Prescription Practices and Their Relationship to Outcome in South African Intensive Care Units: Findings of the Prevalence of Infection in South African Intensive Care Units (PISA) Study. *S Afr Med J* **102**(7)**:** 613-616

Patel DA, Shorr AF, Chastre J, Niederman M, Simor A, Stephens JM*, et al.* (2014). Modeling the Economic Impact of Linezolid Versus Vancomycin in Confirmed Nosocomial Pneumonia Caused by Methicillin-Resistant Staphylococcus aureus. *Crit Care* **18**(4)**:** R157. doi: 10.1186/cc13996

Paul M, Kariv G, Goldberg E, Raskin M, Shaked H, Hazzan R*, et al.* (2010). Importance of Appropriate Empirical Antibiotic Therapy for Methicillin-Resistant Staphylococcus aureus Bacteraemia. *J Antimicrob Chemother* **65**(12)**:** 2658-2665. doi: 10.1093/jac/dkq373

Perovic O, Fortuin-de Smidt M, Chetty V (2014). Antimicrobial Resistance Surveillance from Sentinel Public Hospitals, South Africa, 2013. *Communicable Diseases Surveillance Bulletin* **12**(2)**:** 44-53

Perovic O, Koornhof H, Black V, Moodley I, Dusé A, Galpin J (2006). Staphylococcus aureus Bacteraemia at Two Academic Hospitals in Johannesburg. *S Afr Med J* **96**(8)**:** 714-717

Pharasi B, Miot J (2013). Medicines Selection and Procurement in South Africa: Medicines, Vaccines and Technology. In: Padarath A, English R (eds). *South African Health Review*, 2012/2013 edn. Durban: Health Systems Trust. pp.177-185

Philips Z, Bojke L, Sculpher M, Claxton K, Golder S (2006). Good Practice Guidelines for Decision-Analytic Modelling in Health Technology Assessment: A Review and Consolidation of Quality Assessment. *Pharmacoeconomics* **24**(4)**:** 355-371

Radley DC, Wasserman MR, Olsho LE, Shoemaker SJ, Spranca MD, Bradshaw B (2013). Reduction in Medication Errors in Hospitals Due to Adoption of Computerized Provider Order Entry Systems. *J Am Med Inform Assoc* **20**(3)**:** 470-476. doi: 10.1136/amiajnl-2012-001241

Rascati KL (2013). *Essentials of Pharmacoeconomics*. 2nd edn. Philadelphia: Lippincott Williams & Wilkins. pp.169-192

Rebmann T, Aureden K (2011). Preventing Methicillin-Resistant Staphylococcus aureus Transmission in Hospitals: An Executive Summary of the Association for Professionals in Infection Control and Epidemiology, Inc, Elimination Guide. *Am J Infect Control* **39**(7)**:** 595-598. doi: 10.1016/j.ajic.2010.10.019

Reeves S, Kuper A, Hodges BD (2008). Qualitative Research Methodologies: Ethnography. *BMJ* **337:** a1020. doi: 10.1136/bmj.a1020

Rodriguez-Gonzalez CG, Herranz-Alonso A, Martin-Barbero ML, Duran-Garcia E, Durango-Limarquez MI, Hernández-Sampelayo P*, et al.* (2012). Prevalence of Medication Administration Errors in Two Medical Units with Automated Prescription and Dispensing. *J Am Med Inform Assoc.* **19**(1)**:** 72-78. doi: 10.1136/amiajnl-2011-000332

Safdar N, Narans L, Gordon B, Maki DG (2003). Comparison of Culture Screening Methods for Detection of Nasal Carriage of Methicillin-Resistant Staphylococcus aureus: A Prospective Study Comparing 32 Methods. *J Clin Microbiol* **41**(7)**:** 3163-3166. doi: 10.1128/JCM.41.7.3163-3166.2003

Schellack N, Meyer HJ (2010). Pharmaceutical Ward Stock Management for Nurses. *Prof Nurs Today* **14**(5)**:** 5-10

Schulgen G, Kropec A, Kappstein I, Daschner F, Schumacher M (2000). Estimation of Extra Hospital Stay Attributable to Nosocomial Infections: Heterogeneity and Timing of Events. *J Clin Epidemiol* **53**(4)**:** 409-417. doi: 10.1016/S0895-4356(99)00182-1

Seibert DJ, Speroni KG, Oh KM, DeVoe MC, Jacobsen KH (2014). Preventing Transmission of MRSA: A Qualitative Study of Health Care Workers' Attitudes and Suggestions. *Am J Infect Control* **42**(4)**:** 405-411. doi: 10.1016/j.ajic.2013.10.008

Shittu AO, Lin J (2006). Antimicrobial Susceptibility Patterns and Characterization of Clinical Isolates of Staphylococcus aureus in Kwazulu-Natal Province, South Africa. *BMC Infect Dis* **6:** 125. doi: 10.1186/1471-2334-6-125

Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A*, et al.* (2013). Antimicrobial-Resistant Pathogens Associated with Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. *Infect Control Hosp Epidemiol* **34**(1)**:** 1-14. doi: 10.1086/668770

Solomkin JS, Bjornson HS, Cainzos M, Dellinger EP, Dominioni L, Eidus R*, et al.* (2004). A Consensus Statement on Empiric Therapy for Suspected Gram-Positive Infections in Surgical Patients. *Am J Surg* **187**(1)**:** 134-145. doi: 10.1016/j.amjsurg.2003.03.006

Stephens JM, Gao X, Patel DA, Verheggen BG, Shelbaya A, Haider S (2013). Economic Burden of Inpatient and Outpatient Antibiotic Treatment for Methicillin-Resistant Staphylococcus aureus Complicated Skin and Soft-Tissue Infections: A Comparison of Linezolid, Vancomycin, and Daptomycin. *Clinicoecon Outcomes Res* **5:** 447-457. doi: 10.2147/CEOR.S46991

Tai CC, Nirvani AA, Holmes A, Hughes SP (2004). Methicillin-Resistant Staphylococcus aureus in Orthopaedic Surgery. *Int Orthop* **28**(1)**:** 32-35. doi: 10.1007/s00264-003-0505-2

Tonkin-Crine S, Yardley L, Little P (2011). Antibiotic Prescribing for Acute Respiratory Tract Infections in Primary Care: A Systematic Review and Meta-Ethnography. *J Antimicrob Chemother* **66**(10)**:** 2215-2223. doi: 10.1093/jac/dkr279

TreeAge Software INC (2013). *Treeage Pro 2013 User's Manual*. Williamstown, USA: TreeAge Software, INC

Tübbicke A, Hübner C, Hübner NO, Wegner C, Kramer A, Fleßa S (2012a). Cost Comparison of MRSA Screening and Management - a Decision Tree Analysis. *BMC Health Serv Res* **12:** 438. doi: 10.1186/1472-6963-12-438

Tübbicke A, Hübner C, Kramer A, Hübner NO, Fleßa S (2012b). Transmission Rates, Screening Methods and Costs of MRSA--a Systematic Literature Review Related to the Prevalence in Germany. *Eur J Clin Microbiol Infect Dis* **31**(10)**:** 2497-2511. doi: 10.1007/s10096-012-1632-8

van Hal SJ, Stark D, Lockwood B, Marriott D, Harkness J (2007). Methicillin-Resistant Staphylococcus aureus (MRSA) Detection: Comparison of Two Molecular Methods (IDI-MRSA PCR Assay and GenoType MRSA Direct PCR Assay) with Three Selective MRSA Agars (MRSA ID, MRSASelect, and CHROMagar MRSA) for Use with Infection-Control Swabs. *J Clin Microbiol* **45**(8)**:** 2486-2490. doi: 10.1128/jcm.00139-07

Van Rensburg HCJ (2004). The Health Professions and Human Resources for Health – Status, Trends and Core Issues. In: Van Rensburg HCJ (eds). *Health and Health Care in South Africa*, First edn. Pretoria: Van Schaik Publishers. pp.354-356

Vrijens F, Hulstaert F, Van de Sande S, Devriese S, Morales I, Parmentier Y (2010). Hospital-Acquired, Laboratory-Confirmed Bloodstream Infections: Linking National Surveillance Data to Clinical and Financial Hospital Data to Estimate Increased Length of Stay and Healthcare Costs. *J Hosp Infect* **75**(3)**:** 158-162. doi: 10.1016/j.jhin.2009.12.006

Wassenberg MW, Kluytmans JA, Box AT, Bosboom RW, Buiting AG, van Elzakker EP*, et al.* (2010). Rapid Screening of Methicillin-Resistant Staphylococcus aureus Using PCR and Chromogenic Agar: A Prospective Study to Evaluate Costs and Effects. *Clin Microbiol Infect* **16**(12)**:** 1754-1761. doi: 10.1111/j.1469-0691.2010.03210.x

Wasserman E, Taljaard J (2011). Update on Infections Caused by Staphylococcus aureus. *South Afr J Epidemiol Infect* **26**(2)**:** 60-64

Weinstein MC, O'Brien B, Hornberger J, Jackson J, Johannesson M, McCabe C*, et al.* (2003). Principles of Good Practice for Decision Analytic Modeling in Health-Care Evaluation: Report of the ISPOR Task Force on Good Research Practices—Modeling Studies. *Value Health* **6**(1)**:** 9-17. doi: 10.1046/j.1524-4733.2003.00234.x

Werner EF, Wheeler S, Burd I (2012). Creating Decision Trees to Assess Cost-Effectiveness in Clinical Research. *J Biomet Biostat* **S7:** 004. doi: 10.4172/2155-6180.S7-004

Wertheim HF, Melles DC, Vos MC, van Leeuwen W, van Belkum A, Verbrugh HA*, et al.* (2005). The Role of Nasal Carriage in Staphylococcus aureus Infections. *Lancet Infect Dis* **5**(12)**:** 751-762. doi: 10.1016/s1473-3099(05)70295-4

Wolk DM, Struelens MJ, Pancholi P, Davis T, Della-Latta P, Fuller D*, et al.* (2009). Rapid Detection of Staphylococcus aureus and Methicillin-Resistant S. aureus (MRSA) in Wound Specimens and Blood Cultures: Multicenter Preclinical Evaluation of the Cepheid Xpert MRSA/SA Skin and Soft Tissue and Blood Culture Assays. *J Clin Microbiol* **47**(3)**:** 823-826. doi: 10.1128/JCM.01884-08

World Health Organization (2002). *Prevention of Hospital-Acquired Infections: A Practical Guide*. 2nd edn. Geneva, Switzerland: World Health Organization.

World Health Organization (2009). *WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge, Clean Care Is Safer Care*. Geneva, Switzerland: World Health Organization.

World Health Organization (2014). *Antimicrobial Resistance Global Report on Surveillance*. Geneva, Switzerland: World Health Organization.

World Health Organization Collaborating Centre for Drug Statistics Methodology (2012). *Guidelines for ATC Classification and DDD Assignment 2013*. Oslo, Norway: World Health Organization

World Health Organization Collaborating Centre for Drug Statistics Methodology (2013). *ATC/DDD Index*. Available From: http://www.whocc.no/atc_ddd_index/. Last Updated: 19 December 2013

Yamakawa K, Tasaki O, Fukuyama M, Kitayama J, Matsuda H, Nakamori Y*, et al.* (2011). Assessment of Risk Factors Related to Healthcare-Associated Methicillin-Resistant Staphylococcus aureus Infection at Patient Admission to an Intensive Care Unit in Japan. *BMC Infect Dis* **11:** 303. doi: 10.1186/1471-2334-11-303