THE VALIDATION OF A GUIDELINE ALGORITHM FOR THE ANTIBIOTIC TREATMENT FOR INFECTED LOWER LIMB WOUNDS OR ULCERS
DEDICATION

I would like to dedicate this dissertation first and foremost to my husband Ivan, and to my family for their constant support. Last but not least I would like to dedicate this work to the participants who took part in this study, which would not have been accomplished without their help.
"I did then what I knew how to do. Now that I know better, I do better."

-Maya Angelou
STATEMENT OF AUTHENTICITY

To whom it may concern,

I hereby declare that this dissertation entitled "The validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers.", which I am submitting in partial fulfilment for Masters in Pharmacology and Clinical Pharmacology, is not one for which another Masters has been or will be conferred by this or any other University.

I also confirm that the work for this dissertation and its composition are my own.

Finally I certify that the work for this dissertation has not been presented to any other institution.
THE VALIDATION OF A GUIDELINE ALGORITHM FOR THE ANTIBIOTIC TREATMENT FOR INFECTED LOWER LIMB WOUNDS OR ULCERS.

A dissertation submitted
to the Faculty of Medicine and Surgery
University of Malta
in partial fulfilment of the requirements
for the degree of Masters of Science in Pharmacology and Clinical Pharmacology

Claudine Farrugia

2014
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I would also like to thank my class mates for their support throughout all the stages of this dissertation.

Last but not least I want to express my gratitude to my husband Ivan who provided me with encouragement and continuous support in order to complete this study, to my parents Carmen and Joseph and my brother and sisters, Manuel, Stephanie and Christine for their support during the completion of this study. Without them I would not be where I am now.
# Table of Contents

1. **Chapter 1 Introduction** ........................................................................................................... 1
   
   1.1 Introduction ......................................................................................................................... 2
   1.2 Identifying Wound Infections ............................................................................................... 4
   1.3 Lower Limb Wound Bacterial Flora ...................................................................................... 9
   1.4 Antibiotic Resistance in Lower Limb Wounds and Ulcers ..................................................... 10
   1.5 Antibiotic Use in Malta .......................................................................................................... 11
   1.6 International Lower Limb Wound Antibiotic Guidelines ..................................................... 13
   1.7 Algorithm Developed by Mater Dei Hospital (MDH) Antibiotic Team ................................. 15
   1.8 Antibiotic Treatment and Antibiotics Used in Guidelines ................................................... 19
   1.8.1 Flucloxacin ....................................................................................................................... 20
   1.8.2 Doxycycline ..................................................................................................................... 21
   1.8.3 Clindamycin ..................................................................................................................... 22
   1.8.4 Gentamicin ....................................................................................................................... 24
   1.8.5 Ciprofloxacin ................................................................................................................... 25
   1.9 Identification of Organisms through the Use of Wound Swabs and Culture and Antibiotic Sensitivity Tests ........................................................................................................... 28
   1.9.1 Reliability and Validity of the Culture and Sensitivity Wound Swabs .............................. 29
   1.10 Tool to Assess Vascular Supply: Ankle Brachial Pressure Index (ABPI) ............................ 31
       1.10.1 Reliability and Validity of ABPI .................................................................................... 32
   1.11 Wound Assessment Tool .................................................................................................... 35
       1.11.1 Reliability and Validity of the Bates-Jansen Wound Assessment Tool ......................... 36
   1.12 Factors Affecting Wound Healing ....................................................................................... 37
       1.12.1 Oxygenation and Revascularization ............................................................................ 38
       1.12.2 Steroids ....................................................................................................................... 40
       1.12.3 Antiplatelets and Analgesics ...................................................................................... 40
       1.12.4 Non Insulin Dependent Diabetes Mellitus and Insulin Dependent Diabetes Mellitus ....... 41
   1.13 Aims and Objectives of the Study ....................................................................................... 42

2. **Chapter 2 Methodology** ........................................................................................................... 44
   
   2.1 Research Design and Methods .............................................................................................. 45
   2.2 The Study Procedure ............................................................................................................. 45
   2.3 Observational Non-Experimental Quantitative Study Design ............................................. 47
   2.4 Study Design ......................................................................................................................... 48
       2.4.1 Subject Selection ............................................................................................................. 48
           2.4.1.1 Inclusion and Exclusion Criteria of Patients ......................................................... 49
   2.5 Ethical Considerations .......................................................................................................... 50
   2.6 Data Collection ..................................................................................................................... 51
2.6.1 DATA COLLECTION TOOLS
2.6.2 CULTURE AND SENSITIVITY WOUND SWABS
2.7 WOUND ALGORITHM
2.8 DATA COLLECTION TOOLS
2.8.1 BATES-JENSEN WOUND ASSESSMENT TOOL (BJWAT)
2.8.2 ANKLE BRACHIAL PRESSURE INDEX METHODOLOGY
2.9 SAMPLING
2.10 INFORMED CONSENT
2.11 METHODOLOGY FOR LITERATURE SEARCH
2.12 STATISTICAL ANALYSIS

3. CHAPTER 3 RESULTS

3.1 FOREWORD
3.2 DEMOGRAPHIC DATA
3.3 PATIENT'S CHARACTERISTICS
3.4 WOUND IMPROVEMENT WITH REGARDS TO THE ALGORITHM
3.4.1 COMPLIANCE WITH WOUND ALGORITHM AS DESCRIBED BY THE MATER DEI ANTIBIOTIC TEAM
3.5 RESULTS RELATED TO WOUND SWAB TESTING
3.6 POST-CLEAN OF WOUND TWICE WITH SALINE CULTURE RESULTS
3.7 CONCORDANCE OF WOUND SWABS CULTURE AND SENSITIVITY RESULTS WITH ANTIBIOTICS ADMINISTERED
3.8 OTHER FACTORS WHICH COULD AFFECT WOUND IMPROVEMENT

4. CHAPTER 4 DISCUSSION

4.1 INTRODUCTION
4.2 VALIDATION OF THE LOWER LIMB WOUND AND ULCER ALGORITHM BY MATER DEI ANTIBIOTIC TEAM
4.3 EFFICACY OF WOUND CLEANSING PRIOR TO TAKING A WOUND SWAB
4.4 WOUND MICRO FLORA OBSERVED IN THE STUDY
4.5 CONCORDANCE OF ANTIBIOTICS WITH WOUND IMPROVEMENT
4.6 OTHER FACTORS WHICH MIGHT AFFECT WOUND HEALING
4.6.1 STEROIDS
4.6.2 ANTIPLATELET AND ANALGESICS
4.6.3 OXYGENATION AND REVASCULARIZATION
4.7 INSULIN DEPENDENT DIABETES MELLITUS AND NON INSULIN DEPENDENT DIABETES MELLITUS
4.8 LIMITATIONS OF THE STUDY
4.9 RECOMMENDATIONS FOR FUTURE STUDIES
4.10 RECOMMENDATIONS FOR PRACTICE
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.11 CONCLUSION</td>
<td>118</td>
</tr>
<tr>
<td>5. REFERENCES</td>
<td>120</td>
</tr>
<tr>
<td>6. APPENDIX 1</td>
<td>141</td>
</tr>
<tr>
<td>7. APPENDIX 2</td>
<td>194</td>
</tr>
<tr>
<td>8. APPENDIX 3</td>
<td>199</td>
</tr>
<tr>
<td>9. APPENDIX 4</td>
<td>218</td>
</tr>
<tr>
<td>10. APPENDIX 5</td>
<td>220</td>
</tr>
<tr>
<td>11. APPENDIX 6</td>
<td>225</td>
</tr>
<tr>
<td>12. APPENDIX 7</td>
<td>229</td>
</tr>
<tr>
<td>13.</td>
<td>230</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

Figure 1.1: Signs and symptoms which describe an infection severity as described by the Infectious Disease Society Of America. (Lipsky, 2013) ................................................................. 5

Figure 1.2: A graph indicating the antibiotic prescription in the participating countries (in the EU 27 Member States) between 2009 and 2013 (Special Eurobarometer 407 Antibiotic Resistance) (were yes: antibiotic prescribed, no: no antibiotics prescribed) ........................................................................... 11

Figure 1.3: The whole algorithm as identified by the MDH antibiotic team (Guideline algorithm for the antibiotic treatment of common infectious diseases in the hospital setting, 2012) ........................................... 18

Figure 1.4: A graph showing the prescription pattern in the General Practice Morbidity Database (GPDM) (Howell-Jones et al., 2006), where FLU, flucloxacillin, AMX, amoxicillin: AMC, co-amoxiclav; CEC, cefaclor: LEX, cefalexin; DOX, doxycycline; ERY, erythromycin; TMP, trimethoprim; MRZ, metronidazole; CIP, ciprofloxacin ...................................................... 20

Figure 1.5: A flow diagram indicating the factors which might influence tissue hypoxia, (Schreml et al, 2010) ...................................................... 39

Figure 2.1: A flow diagram outlining the method used for data collection ................................................................. 46

Figure 2.2: The formula used to calculate the ABPI ................................................................................................. 55

Figure 2.3: A flow diagram indicating the Levine technique which was used for obtaining the wound swab for culture and sensitivity (Angel et al, 2011) .................................................................................. 56

Figure 2.4: A figure indicating the methodology adopted for taking a wound swab. (Patten, 2010) 57

The wound swabs collected were tested at Mater Dei Hospital Pathology lab. As a policy, if the lab cultures more than three microbes from a single wound swab, the result would conclude a mixed culture, and no identification of the microbes and their sensitivities would be available . . . 58

Figure 2.5: This figure describes the whole algorithm as identified by the MDH antibiotic team (Guideline algorithm for the antibiotic treatment of common infectious diseases in the hospital setting, 2012) ................................................................................................................................. 61

Figure 2.6: A diagram indicating the method used to measure undermining of the wound. (Wound Assessment, 2014) ................................................................. 62

Figure 3.1: A bar graph indicating the number of participants according to the Ankle Brachial Pressure Index (ABPI). ................................................................................. 72

Figure 3.2: Represents a flow diagram indicating a summary of how the patients were divided. Where NS/HR; Non-Severe wound infection (WI) / High Risk, NS/LR; Non-Severe WI/ Low Risk, HR/S; High Risk/ Severe WI, LR/S; Low risk/ Severe WI, Y; Concordant with wound swab sensitivity result post- clean, N; No concordance with wound swab sensitivity result post clean, P; Partial concordance with wound swab sensitivity result post- clean, N/A; No information given with regard to wound swab sensitivity result post clean. .................................................. 74

Figure 3.3: A bar graph indicating the number of organisms identified from wound swabs pre cleaning twice with saline, and post cleaning twice with saline as advised by the guidelines (Three participants are included in this table, which were not included in the study population as they presented with no organisms in the post clean wound swab result, hence indicating no infection). 86

Figure 3.4: A pie chart indicating the percentage of groups of micro organisms identified in the post-cleaning of the wound twice with saline as advised by the MDH Antibiotic team............................... 92
LIST OF TABLES

TABLE 1.1: INDICATORS FOR INFECTION AS DESCRIBED BY CUTTING AND WHITE 2004, USING A DELPHI APPROACH. ........................................... 7

TABLE 1.2: THE CRITERIA FOR SEVERITY OF A WOUND AS DESCRIBED BY THE WOUND ALGORITHM FOR INFECTED LOWER LIMB WOUNDS OR ULCERS BY MDH ANTIBIOTIC TEAM (GUIDELINE ALGORITHM FOR THE ANTIBIOTIC TREATMENT OF COMMON INFECTIOUS DISEASES IN THE HOSPITAL SETTING, 2012) .......................................................... 8

TABLE 1.3: A DESCRIPTION OF VARIOUS FOREIGN ALGORITHMS OR GUIDELINES FOR THE TREATMENT OF INFECTED LOWER LIMB WOUNDS. ........................................................................................................ 14

TABLE 1.4: THE ANTIBIOTICS USED IN THE ALGORITHM FOR LOWER LIMB WOUNDS AND ULCERS DEVELOPED BY MATER DEI HOSPITAL. (GUIDELINE ALGORITHM FOR THE ANTIBIOTIC TREATMENT OF COMMON INFECTIOUS DISEASES IN THE HOSPITAL SETTING, 2012) .................................................................... 16

TABLE 1.5: A SUMMARY TABLE SHOWING THE ACTION OF THE ANTIBIOTICS AND THEIR EFFECT ON MRSA ........................................ 27

TABLE 1.6: A TABLE INDICATING THE VALUES WHICH COULD BE OBTAINED WHEN PERFORMING THE ABPI AND THEIR MEANING...... 31

TABLE 1.7: VARIABLES WHICH MUST BE CONSIDERED AND ACCOUNTED FOR PRIOR TO INTERPRETING ABPI RESULTS (ADAPTED FROM KEEN, 2008) .................................................................................. 33

TABLE 1.8: ADVANTAGES AND DISADVANTAGES OF ABPI MEASUREMENT (ADAPTED FROM CAD ET AL, 2011) ................................. 34

TABLE 1.9: A DIAGRAM IDENTIFYING FACTORS WHICH CAN ADVERSELY AFFECT WOUND IMPROVEMENT. (ADAPTED FROM HOLMES AND NORMAN, 2008) ................................................................. 37

TABLE 2.1: A TABLE IDENTIFYING THE METHOD USED TO OBTAIN THE BRACHIAL SYSTOLIC PRESSURE WHICH WILL BE USED FOR ABPI. 53

TABLE 2.2: A TABLE IDENTIFYING THE METHOD USED TO OBTAIN THE ANKLE SYSTOLIC PRESSURE WHICH WILL BE USED FOR ABPI. 54

TABLE 2.3: A TABLE INDICATING THE TWO SECTIONS OF THE GUIDELINES ALGORITHM WHICH WERE USED IN THIS STUDY .............. 59

TABLE 2.4: THIS TABLE DESCRIBES THE CRITERIA FOR IDENTIFYING NON-SEVERE AND SEVER WOUNDS. ................................................. 60

TABLE 2.5: A TABLE INDICATING THE STAGES OF NECROTIC TISSUE TYPE. ................................................................. 63

TABLE 2.6: A TABLE INDICATING THE RATING VALUE OBTAINED IN THE BJWAT AND THE INDICATION OF WOUND SEVERITY .......... 65

TABLE 3.1: THE AGE GROUPS AND THE NUMBER OF PARTICIPANTS IN EACH AGE GROUP. ................................................................. 72

TABLE 3.2: THE NUMBER OF PARTICIPANTS BEING DIABETIC ON INSULIN, OR ON ORAL ANTI-DIABETIC AGENTS, OR DIET, AND NON- DIABETICS. ....................................................................................... 73

TABLE 3.3: A TABLE INDICATING THE NUMBER OF PARTICIPANTS BEING HIGH/ LOW RISK, SEVERE/ NON-SEVERE .................. 73

TABLE 3.4: INDICATES THE PARAMETERS OF THE BJWAT, THE MEAN WOUND IMPROVEMENT AND THE P-VALUE OBTAINED FOR ALL PARTICIPANTS. ................................................................. 76

TABLE 3.5: A TABLE INDICATING THE WOUND IMPROVEMENT (MEAN REDUCTION IN BJWAT SCORE) WITH COMPLIANCE TO ALGORITHM ........................................................................................................ 77

TABLE 3.6: A TABLE INDICATING THE MEAN IMPROVEMENT IN WOUND (REDUCTION IN BJWAT SCORE) WITH RISK FOR ANTIBIOTIC RESISTANCE. ................................................................. 78

TABLE 3.7: A TABLE INDICATING THE MEAN WOUND IMPROVEMENT (REDUCTION IN BJWAT SCORE) WITH SEVERITY OF WOUND INFECTION. ........................................................................................................ 78

TABLE 3.8: A TABLE INDICATING THE MEAN WOUND IMPROVEMENT (REDUCTION IN BJWAT) WITH SEVERITY OF WOUND AND WITH ANTIBIOTIC RESISTANCE RISK. ........................................ 79

TABLE 3.9: POST- HOC TESTS FOR WOUND IMPROVEMENT WITH RISK FOR ANTIBIOTIC RESISTANCE AND SEVERITY OF WOUND. ...... 79

TABLE 3.10: A TABLE INDICATING THE GENERAL LINEAR MODEL RESULT FOR SEVERITY OF WOUND AND RISK FOR ANTIBIOTIC RESISTANCE ........................................................................................................ 80

TABLE 3.11: A TABLE INDICATING THE INDIVIDUALS WHO WERE COMPLIANT OR NON-COMPLIANT WITH THE ALGORITHM WITH REGARDS TO THE SEVERITY AND RISK PARAMETERS ................. 81

TABLE 3.12: A TABLE INDICATING THE MEAN WOUND IMPROVEMENT IN THOSE PATIENTS WHO WERE COMPLIANT OR NON-COMPLIANT ACCORDING TO THE WOUND SEVERITY AND RISK FOR ANTIBIOTIC RESISTANCE ........................................................................................................ 82
TABLE 3.13: A table indicating the effects of compliance on risk and severity parameters. ........................................... 83
TABLE 3.14: A table indicating the significant difference between compliance and severity of wound parameters. ...... 84
TABLE 3.15: A table indicating the significant difference between compliance and risk to antibiotic resistance parameters. ........................................................................................................... 84
TABLE 3.16: A table indicating the general linear model analysis result for compliance and severity/risk parameters. .................................................................................................................................................. 84
TABLE 3.17: A table indicating the difference in the total number of organisms pre-cleaning of the wound and post cleaning of the wound. .................................................................................................................. 85
TABLE 3.18: A table indicating the results obtained between post-cleaning of a wound with saline and risk for antibiotic resistance ........................................................................................................................................... 89
TABLE 3.19: A table indicating the significance of microbes identified post-cleaning of the wound with the severity of wound infection and risk for antibiotic resistance. ................................................................................................. 90
TABLE 3.20: A table indicating all the species present in the post-clean wound swab. ...................................................... 91
TABLE 3.21: A table indicating the wound improvement with compliance to wound swab sensitivity result. (Were yes: concordant with wound swab results, no: not concordant with wound swab results, partial: that there was partial concordance with wound swab results, and not available: that no sensitivity results were achieved, as culture result obtained was highly mixed, hence no sensitivities were present). .................................................................................................................. 94
TABLE 3.22: A table indicating the number of individuals who were concordant with the wound swab sensitivity results in view of severity and risk parameters and the p-value obtained. Where HR: high risk, S: severe, LR: low risk, NS: non-sever. .................................................................................................................................................. 95
TABLE 3.23: A table indicating a general linear model for compliance with algorithm, concordance with wound swab posts clean and number of organisms in post-clean wound swabs. .................................................................................................................. 96
TABLE 3.24.1: A table indicating the mean values and p-values for other factors which might have influenced the wound improvement (Part One). .................................................................................................................. 97
TABLE 3.24.2: A table indicating the mean values and p-values for other factors which might have influenced the wound improvement (Part 2). .................................................................................................................. 98
TABLE 3.25: A table indicating the general linear model for revascularization procedure and four layer bandage as treatment modalities. .................................................................................................................. 99
TABLE 3.26: A table indicating the general linear model for IDDM (Insulin dependent Diabetes Mellitus) and NIDDM (Non-insulin dependent Diabetes Mellitus). .................................................................................. 100
# List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ABPI</td>
<td>Ankle brachial Pressure Index</td>
</tr>
<tr>
<td>AMC</td>
<td>Co- amoxiclav</td>
</tr>
<tr>
<td>AMX</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>BJWAT</td>
<td>Bates Jensen Wound Assessment Tool</td>
</tr>
<tr>
<td>C&amp;S</td>
<td>Culture and Sensitivity wound swab</td>
</tr>
<tr>
<td>CEC</td>
<td>Cefaclor</td>
</tr>
<tr>
<td>CIP</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>DOX</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>ERY</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>FLU</td>
<td>Flucloxacillin</td>
</tr>
<tr>
<td>GPMD</td>
<td>General Practice Morbidity Database</td>
</tr>
<tr>
<td>HR</td>
<td>High Risk for antibiotic resistance</td>
</tr>
<tr>
<td>IDDM</td>
<td>Insulin Dependent Diabetes Mellitus</td>
</tr>
<tr>
<td>LR</td>
<td>Low Risk for antibiotic resistance</td>
</tr>
<tr>
<td>MDH</td>
<td>Mater Dei Hospital</td>
</tr>
<tr>
<td>MRSA</td>
<td>Methicillin Resistant <em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>MRZ</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>N</td>
<td>No concordance with wound swab result</td>
</tr>
<tr>
<td>N/A</td>
<td>No available concordance with wound swab result</td>
</tr>
<tr>
<td>NIDDM</td>
<td>Non Insulin Dependent Diabetes Mellitus</td>
</tr>
<tr>
<td>NS</td>
<td>Non- Severe infection</td>
</tr>
</tbody>
</table>
ORSA  Oxacillin Resistant *Staphylococcus aureus*

P  Partial concordance with wound swab result

PSST  Pressure Score Status Tool

S  Severe infection

SOP  Surgical Out Patients

Spp  Species

SVPR  St. Vincent De Paul Residence for the elderly

TMP  Trimethoprim

TVU/TVC  Tissue Viability Unit/ Tissue Viability Clinic

UREC  University Research Ethics Committee

Y  Yes concordant with wound swab result
ABSTRACT

Lower limb and foot ulcers are a common complication arising from multiple causative factors including peripheral vascular disease, excessive pressure and neuropathy. Pharmacological management is introduced if an infection is present. Infections are identified through clinical manifestations (signs and symptoms). These include erythema, pus, cellulitis and malodour amongst others. Moreover in order to appropriately treat a wound infection through the use of antibiotics, it is necessary to correctly identify the infecting organisms, through the use of culture testing. Antibiotic guidelines are used in order to aid practitioners administering the correct antibiotics to treat infections. In fact the Antibiotic Team at Mater Dei Hospital (MDH) the main teaching hospital in Malta have created an algorithm for lower limb wound infections and ulcers. The aim of this study was to assess and validate this algorithm. In addition, other secondary objectives were identified such as the importance of proper cleaning of a wound prior to taking a wound swab, identifying the importance of proper antibiotic treatment, exploring the relationship between the Ankle Brachial Pressure Index (ABPI) and wound improvement, and identifying any other parameters which might be implicated in wound improvement.

To achieve these aims, 80 patients were identified who fulfilled the inclusion and exclusion criteria through non-probability sampling. Patients were selected from MDH Surgical Out- Patients, MDH Tissue Viability Clinic, and St Vincent De Paul Residence for the elderly (SVPR). The methodology used included, first and foremost, obtaining informed consent from the selected patient following patient selection. Demographic data of the patient was then performed using a specific form designed by the researcher. A wound swab
for culture and sensitivity was taken from the wound pre-cleaning and post-cleaning twice with saline as advised by the antibiotic team. The Levine technique was the method employed to take the wound swab. The Bates Jensen Wound Assessment Tool (BJWAT) was then filled up by the researcher. The Ankle Brachial Pressure Index, (ABPI) was then calculated, and patients were administered antibiotics by the doctor according to the algorithm. Patients were then assessed during two more visits, where the BJWAT and the demographic data were filled on each occasion as required to monitor wound improvement. Following data collection, the patients were classified according to risk for antibiotic infection and for severity of wound infection.

Analysis of the results indicate that the algorithm created by the MDH antibiotic team was validated, with a $p$-value of <0.001 in all the parameters of the BJWAT. Results indicate a $p$-value of 0.010 for wound improvement in those individuals who were compliant versus those non-compliant with the algorithm. Results also indicate that wound cleaning is imperative for proper identification of wound bacterial flora. In fact findings showed that the highly mixed cultures decreased from 38 to 4 individuals from pre-cleaning to post-cleaning. Moreover, the importance of wound cleaning was evident since, a statistically significant result with a $p$-value of < 0.001 was obtained for difference in number of organisms pre-cleaning and post-cleaning.

ABPI was found to be important for wound improvement, as individuals who had a decreased ABPI and who have had a revascularization procedure, obtained better mean results, even though no significant $p$-value was obtained.

Other parameters which were found to effect wound improvement were steroids, antiplatelet drugs, analgesics, and IDDM and NIDDM.
Hence it can be concluded that the algorithm is validated. Moreover this study highlights also the importance of proper wound cleansing prior to taking a wound swab in order to identify the true infecting organisms. This study will be of benefit to patients and also to stakeholders, in reducing the unnecessary use of inappropriate antibiotics, which increase antibiotic resistance and also reduces medical costs of unnecessary antibiotic administration and hospital stays. Moreover this study highlights the importance for a protocol for proper wound swabbing technique, for the identification of infecting microorganisms, which will in turn, increase the reliability and validity of wound swabbing hence guiding appropriate antibiotic treatment.
CHAPTER 1

INTRODUCTION
1.1 **INTRODUCTION**

Lower limb and foot ulcers are a common complication worldwide. These wounds are due to several causative factors which can be multi-factorial and include, amongst others, excessive pressure, loss of peripheral vascularity, and neuropathy (Gist *et al.*, 2009).

Antibiotic administration constitutes part of the treatment management plan, if an infection is diagnosed in a lower limb wound or ulcer. It is very important for an infection to be diagnosed as early as possible in order to avoid complications including osteomyelitis (Copobianco and Stapelton, 2010). It is also important to identify the organisms present in the lesion in order to be able to provide the individual with appropriate antibiotic treatment against the offending organism (Bowering, 2001).

Multiple guidelines or algorithms have been developed which guide practitioners in their respective healthcare settings in treating such wound infections. These guidelines have been formulated from evidence based data available in peer reviewed literature (e.g. Del Pozo *et al.*, 2009, Flavia *et al.*, 2012, Vidillac *et al.* 2011, Alonge *et al.*, 2002). However no published studies have been found indicating whether combinations of antibiotics are effective in such scenarios.

The main general teaching hospital in Malta, Mater Dei Hospital (MDH), has identified the need to assist practitioners in their use of antibiotics. Hence an antibiotic algorithm to be used as a prescribing guideline was introduced by the MDH Antibiotic Team in 2012 and it provides guidelines as to which antibiotics to use in specific bacterial
infections. In this specific study, the focus was on the section of the algorithm which describes the antibiotics to be used for infected lower limb wounds.

Indeed the main aim of this study is to validate this algorithm for lower limb wound or ulcers in Malta.

This validation was carried out through the assessment of the improvement in a wound, through the use of a wound assessment tool, following culture and sensitivity swab tests and the administration of antibiotics for infected lower limb wounds and ulcers.

This introductory chapter, reviews published peer reviewed literature which has studied the following aspects relevant to this study:

1. Signs and symptoms which will aid the practitioner in identifying lower limb wound infections.
2. Typical wound bacterial flora found in lower limb wound and ulcers.
3. Antibiotics used in recommended algorithms or guidelines in various health care settings, and studies which describe the effectiveness of such algorithms assessed.
4. The importance of wound cleansing prior to wound swabbing for culture and sensitivity testing.
5. Other factors which might influence wound improvement apart from antibiotics.
6. Ankle Brachial Pressure Index (ABPI) and its use in identifying vascular disease.
1.2 IDENTIFYING WOUND INFECTIONS.

Diagnosing a wound infection is necessary in order to avoid administering unnecessary antibiotics and thus increasing the likelihood of antibiotic resistance (Calne, 2005). The Infectious Disease Society of America provides guidelines for the classification of Diabetic Wound Infections in the lower limbs (Figure 1.1).
Figure 1.1: Signs and symptoms which describe an infection severity as described by the Infectious Disease Society of America (Lipsky, 2013).

<table>
<thead>
<tr>
<th>Clinical Manifestation of Infection</th>
<th>A diagram indicating the wound type</th>
</tr>
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<tbody>
<tr>
<td><strong>Uninfected</strong></td>
<td></td>
</tr>
<tr>
<td>No symptoms or signs of infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td><img src="image.png" alt="Uninfected" /></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mild Infection</strong></th>
<th><img src="image.png" alt="Mild Infection" /></th>
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<tbody>
<tr>
<td>Local infection involving only the skin and subcutaneous tissue</td>
<td></td>
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<tr>
<td>Erythema &gt;0.5cm - &lt;2cm</td>
<td></td>
</tr>
<tr>
<td>Exclude other causes of inflammatory response of the skin (eg: trauma, gout, fracture)</td>
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<th><strong>Moderate Infection</strong></th>
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<tr>
<td>Local infection with erythema &gt;2cm or involving structures deeper than the skin and subcutaneous tissue (eg: osteomyelitis)</td>
<td></td>
</tr>
<tr>
<td>No systematic inflammatory response signs</td>
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<tr>
<th><strong>Severe Infection</strong></th>
<th><img src="image.png" alt="Severe Infection" /></th>
</tr>
</thead>
<tbody>
<tr>
<td>Local infection with the signs of systemic inflammatory response, as manifested by ≥ 2 of the following</td>
<td></td>
</tr>
<tr>
<td>Temperature &gt;38°C or &lt;36°C</td>
<td></td>
</tr>
<tr>
<td>Heart rate &gt;90 beats/ minute</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate &gt;20 breaths/ minute</td>
<td></td>
</tr>
<tr>
<td>White blood cell count &gt;12000 or &lt;4000 cell/mm³ or 10% immature (band) forms</td>
<td></td>
</tr>
</tbody>
</table>
The Delphi Approach (which is a method where a consensus is reached through group/panel response) conducted by Cutting and White, 2004 classified the indicators which ranked a mean score of 8-9, (i.e. in the high key in Table 1.1) as diagnostic features of infection, whilst, those with a criteria ranking 4-5, (i.e. the low key in Table 1.1) can be considered as signposts of infection, and the ones with ranking 6-7, (i.e. the medium key in Table 1.1) as indicators of subtle infection (Calne, 2005).

Whilst the Delphi process has identified the criteria for infection in six types of wounds, for the purpose of the study only five types of ulcers seen with foot infections were included in this review, specifically:

1. Diabetic foot ulcers
2. Arterial Leg Ulcers
3. Venous leg ulcers
4. Pressure Ulcers.
5. Neuropathic ulcers
Table 1.1: Indicators for infection as described by Cutting and White 2004, using a Delphi approach.

<table>
<thead>
<tr>
<th>Key</th>
<th>Diabetic Foot Ulcers</th>
<th>Arterial Leg Ulcers</th>
<th>Venous Leg Ulcers</th>
<th>Pressure Ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIGH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Cellulitis</td>
<td>• Cellulitis</td>
<td>• Cellulitis</td>
<td>• Cellulitis</td>
</tr>
<tr>
<td></td>
<td>• Lymphangitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Phlegmorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Purulent exudate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pus/ abscess</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MEDIUM</strong></td>
<td>• Crepitus in the joint</td>
<td>• Change in colour/ viscosity of exudate</td>
<td>• Delayed healing</td>
<td>• Change in nature of pain</td>
</tr>
<tr>
<td></td>
<td>• Erythema</td>
<td>• Change in wound bed colour</td>
<td>• despite appropriate compression therapy</td>
<td>• Crepitus</td>
</tr>
<tr>
<td></td>
<td>• Fluctuation</td>
<td>• Crepitus</td>
<td>• Increased local skin temperature</td>
<td>• Increase in exudates</td>
</tr>
<tr>
<td></td>
<td>• Increase exudate volume</td>
<td>• Deterioration of wound</td>
<td>• Increase in ulcer pain</td>
<td>• Pus</td>
</tr>
<tr>
<td></td>
<td>• Induration</td>
<td>• Dry necrosis turning wet</td>
<td>• Newly formed ulcers</td>
<td>• Serous exudates with inflammation</td>
</tr>
<tr>
<td></td>
<td>• Localised pain in a normally asensate foot</td>
<td>• Increase in local skin temperature</td>
<td>• Wound bed extension</td>
<td>• Spreading erythema</td>
</tr>
<tr>
<td></td>
<td>• Malodour</td>
<td>• Lymphangitis</td>
<td>• with inflamed margins</td>
<td>• Viable tissue becomes sloughy</td>
</tr>
<tr>
<td></td>
<td>• Probe to bone</td>
<td>• Malodour</td>
<td></td>
<td>• Warmth in surrounding tissues</td>
</tr>
<tr>
<td></td>
<td>• Unexpected pain/ tenderness</td>
<td>• Necrosis- new or spreading</td>
<td></td>
<td>• Wound stops healing despite relevant measures</td>
</tr>
<tr>
<td><strong>LOW</strong></td>
<td>• Blue- Black discolouration and haemorrhage</td>
<td>• Erythema</td>
<td>• Discolouration</td>
<td>• Enlarging wound despite pressure relief</td>
</tr>
<tr>
<td></td>
<td>• Bone or tendon becomes exposed at base of ulcer</td>
<td>• Erythema in per- ulcer tissue- persists with leg elevation</td>
<td>• Friable granulation</td>
<td>• Erythema</td>
</tr>
<tr>
<td></td>
<td>• Delayed/ arrest of wound healing despite offloading and debridement</td>
<td>• Fluctuation</td>
<td>• Increase in exudate viscosity and volume</td>
<td>• Friable granulation tissue that bleeds easily</td>
</tr>
<tr>
<td></td>
<td>• Deterioration of wound</td>
<td>• Increase in exudate volume</td>
<td>• Malodour</td>
<td>• Malodour</td>
</tr>
<tr>
<td></td>
<td>• Friable granulation tissue that bleeds easily</td>
<td>• Increase in size in a previously healing ulcer</td>
<td>• Dusky wound hue</td>
<td>• Oedema</td>
</tr>
<tr>
<td></td>
<td>• Local oedema</td>
<td>• Increased pain</td>
<td>• Sudden appearance / increase in amount of slough</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Sinuses develop in an ulcer</td>
<td>• Ulcer breakdown</td>
<td>• Sudden appearance of necrotic black spots</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Spreading necrosis/ gangrene</td>
<td></td>
<td>• Ulcer enlargement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ulcer base changes from healthy pink to yellow or grey</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The criteria for wound severity provided in the lower limb wounds or ulcers algorithm derived by the MDH antibiotic team (Table 1.2) are very similar to the criteria described in Figure 1.1 and Table 1.1. These criteria thus further aid practitioners in stratifying the patients and hence giving them more appropriate antibiotics.

Table 1.2: The criteria for severity of a wound as described by the wound algorithm for infected lower limb wounds or ulcers by MDH Antibiotic Team (Guideline algorithm for the antibiotic treatment of common infectious diseases in the hospital setting, 2012).

<table>
<thead>
<tr>
<th>Infection severity</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colonisation</strong></td>
<td>No systemic illness</td>
</tr>
<tr>
<td></td>
<td>No presence of pus or signs of inflammation</td>
</tr>
<tr>
<td></td>
<td>Culture of pathogenic bacteria</td>
</tr>
<tr>
<td><strong>Non-Severe Infection</strong></td>
<td>No fever</td>
</tr>
<tr>
<td></td>
<td>Presence of pus or two or more signs of inflammation including erythema, warmth,</td>
</tr>
<tr>
<td></td>
<td>pain and tenderness</td>
</tr>
<tr>
<td></td>
<td>Infection confined to subcutaneous tissue, cellulitis, &lt;2 cm surrounding wound</td>
</tr>
<tr>
<td><strong>Severe Infection</strong></td>
<td>Fever±</td>
</tr>
<tr>
<td></td>
<td>Presence of</td>
</tr>
<tr>
<td></td>
<td>Lymphatic streaking</td>
</tr>
<tr>
<td></td>
<td>Deep tissue infection</td>
</tr>
<tr>
<td></td>
<td>Abscess</td>
</tr>
<tr>
<td></td>
<td>Cellulitis &gt; 2 cm surrounding wound</td>
</tr>
<tr>
<td><strong>Life threatening</strong></td>
<td>Any infection accompanied by systemic toxicity (chills, fever, shock, vomiting,</td>
</tr>
<tr>
<td>infection</td>
<td>confusion, metabolic instability)</td>
</tr>
<tr>
<td></td>
<td>Presence of critical ischemia of involved limb</td>
</tr>
</tbody>
</table>
1.3 LOWER LIMB WOUND BACTERIAL FLORA

Following the identification of infection, it is important to identify the infecting organisms, and thus treat with appropriate antibiotics. For this purpose, multiple studies have been conducted to determine the bacterial flora present in wounds in the lower limb and foot ulcers, especially in diabetic foot ulcers. In a study conducted by Diamantopoulos et al, 1998, it was observed that the majority of the wounds presented with multiple microbes, with an average of 2.8 species (Diamantopoulos et al, 1998 and Price et al, 2009). In this study, it was also concluded that a ratio of 3:1 could be observed when a wound was assessed for aerobic: anaerobic micro-organisms. Prevalence studies indicated that the wound flora examined contained more aerobe bacteria (Diamantopoulos et al, 1998). This was also noted by Calhoun et al, 2002. Eleftheriadou et al, 2010, also described an increased prevalence of Methicillin-resistant Staphylococcus aureus (MRSA) in hospitalised individuals which amounted between 15-30% of infected foot ulcers, depending on the location of the hospital (Eleftheriadou et al, 2010).

Such studies have confirmed that wounds are inhibited by multiple organisms, and these in turn increase the risk of infection. Infection is diagnosed if there is purulent exudate present from the wound, or if there are any two or more signs of inflammation present from: redness in the skin surrounding the wound, pain, tenderness, warmth surrounding the wound (Hobizal and Wukich, 2012). These signs could determine why wounds develop into a chronic state from an acute state. This is partially due to an inappropriate antibiotic regimen which could eradicate bacteria in a wound (Dr. Bjarnsholt et al, 2008). Hence this emphasises the importance of the appropriate use of a rigorous antibiotic regimen at an appropriate time.
Following treatment with antibiotics, for systemic, acute or local infections, a bacterial balance is achieved. Once bacterial balance in a wound is achieved, antibiotic treatment should be stopped, as this may hinder the wound healing and increase the resistance of organisms (Werlin et al., 2009).

1.4 ANTIBIOTIC RESISTANCE IN LOWER LIMB WOUNDS AND ULCERS

Inappropriate use of antibiotics increases, the development of resistant organisms hence introducing a problem in treating resistant microbes. (Ambrosi et al., 2011). This is due to the fact that multiple organisms undergo changes and build up a cross resistance to a broad spectrum of antibiotics. One example is *Pseudomonas aeruginosa*, whose strains are most frequently sensitive to cephalosporins, carbenicillin, gentamicin, polymyxin, fluoroquinolones, but, reports indicated an tendency for cross resistance (Sivanmaliappan and Sevanan, 2011). Similar trends have also been described for *Staphylococcus aureus*, especially MRSA, where in a study conducted by Parvez et al., 2012 it was indicated that 30% of the *Staphylococcus aureus* organisms cultivated from specimens, were MRSA and, the latter together with all the *Enterococcus* isolates exhibited sensitivity for vancomycin. On the other hand, Howell and Goulston, 2011, indicated that there is an increase in resistance which could make vancomycin ineffective towards MRSA microbes.
1.5 **ANTIBIOTIC USE IN MALTA**

Avoidable antibiotic prescriptions might result in antibiotic resistance, hence it is advisable, to use antibiotics with responsibility. A European survey estimated that, 48% of the Maltese participants have been prescribed antibiotics for various reasons. (Special Eurobarometer 407 Antibiotic Resistance)

The Eurobarometer survey found that the number of Europeans, who have been prescribed antibiotics in 2013, decreased by 5% (from 40% to 35%) as shown in Figure 1.2 (Special Eurobarometer 407 Antibiotic Resistance)

![Graph showing antibiotic prescription rates from 2009 to 2013](image)

**Figure 1.2**: A graph indicating the antibiotic prescription in the participating countries (in the EU 27 Member States) between 2009 and 2013 (Special Eurobarometer 407 Antibiotic Resistance) (were yes: antibiotic prescribed, no: no antibiotics prescribed).
This study has also identified certain traits such as the fact that women were more likely to have taken antibiotics. Educational background was not found to affect the likelihood of taking antibiotics, whilst a secure economic circumstance does play a role in the likelihood of taking antibiotics (Special Eurobarometer 407 Antibiotic Resistance). Seven percent of those participating in this survey had used antibiotics in order to treat skin or wound infection (an increase of 2% from 2009). It was also highlighted that participants who were younger were more likely to use antibiotic in treating illnesses, for which antibiotics are not indicated (Special Eurobarometer 407 Antibiotic Resistance). This fact does increase the chance of antibiotic resistance making them ineffective when truly required.

In order to avoid antibiotic resistance as described above it is important to identify infection and identify also the sensitivities of the organisms. Antimicrobial use has been assessed in Malta, in a study by Zarb and Borg in 2011. Data from 2007 up till 2009 indicated that the use of antibiotics had increased from 18.6% up to 24.4% in 3 years. This increase was recorded even though a huge campaign has been undertaken in the previous three years against the administration of over the counter antibiotics.

According to a report by the World Health Organisation (WHO) in 2004, Malta was found to have the lowest antimicrobial resistance rate in comparison to, Greece and, Israel (the only 3 Mediterranean countries compared). Antimicrobial resistance has been estimated to cause a loss of 1.5 billion Euros per year in the European Union Member States, hence highlighting the excessive burden on European countries resulting from antimicrobial resistance. (WHO, 2004).
1.6 **INTERNATIONAL LOWER LIMB WOUND ANTIBIOTIC GUIDELINES**

Several countries, as already described, have formulated algorithms or guidelines which assist the prescribers in various health care settings to effectively treat lower limb wound infections. In fact multiple health care providers have established their own guidelines. Some of which, are being described in Table 1.3 below. Other examples of algorithms are also found in Appendix 1.
Table 1.3: A description of various foreign algorithms or guidelines for the treatment of infected lower limb wounds.

<table>
<thead>
<tr>
<th>Hospital/Trust</th>
<th>Infection Severity</th>
<th>Likely organisms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Royal Devon and Exeter</td>
<td>Mild Infection</td>
<td>Usually Monomicrobial with <em>Staphylococcus aureus</em> or β-haemolytic streptococci. May be polymicrobial if individual had previous antimicrobial treatment.</td>
<td>Flucloxacillin, if penicillin allergic: co-trimoxazole.</td>
</tr>
<tr>
<td>Antimicrobial Stewardship Group, (2012)</td>
<td>Moderate Infection</td>
<td>Usually polymicrobial with <em>Staphylococcus aureus</em> or β-haemolytic streptococci. If individual had previous antimicrobial treatment, Gram-ve organisms can be present.</td>
<td>co- Amoxiclav , if penicillin allergic: clindamycin, if MRSA: vancomycin</td>
</tr>
<tr>
<td></td>
<td>Severe Infection</td>
<td>Polymicrobial Gram +ve/-ve, including anaerobes.</td>
<td>clindamycin and piperacillin- tazobactam, If penicillin allergic: clindamycin and ciprofloxacin, and if MRSA : vancomycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cork University Hospital Shah et al, 2011</td>
<td>Severe sepsis</td>
<td>Polymicrobial Gram +ve/-ve, including anaerobes</td>
<td>clindamycin and piperacillin-tazobactam if MRSA : vancomycin</td>
</tr>
<tr>
<td></td>
<td>Cellulitis</td>
<td><em>Staphylococcus aureus</em> and Streptococci</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gas Gangrene</td>
<td><em>Clostridium perfringens</em> and other gas producing organisms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surgical Wound Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic foot infection: superficial ulcer</td>
<td>Often polymicrobial, occasionally including MRSA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic foot infection: Deep ulcer leading to tendon, bone or joint capsule</td>
<td>Often polymicrobial, occasionally including MRSA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deep ulcer plus active cellulitis</td>
<td>Often polymicrobial, occasionally including MRSA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cellulitis</td>
<td>Usually β- Haemolytic Streptococci and MSSA</td>
<td></td>
</tr>
<tr>
<td>Antibiotic Guidelines 2013-2014 Treatment Recommendations for Adults (Cosgrove, Aydic, 2013)</td>
<td>Suppurative cellulitis</td>
<td>MSSA OR MRSA</td>
<td>TMP/SMX or doxycycline or clindamycin or vancomycin</td>
</tr>
<tr>
<td></td>
<td>Diabetic foot infections: Mild</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic foot infections: Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic foot infections: Severe</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic foot infections: Mild</td>
<td>cephalasine or amoxicillin/ clavulanate or clindamycin in penicillin allergy.</td>
</tr>
<tr>
<td>Diabetic foot infections: Moderate</td>
<td>cephalasine or amoxicillin/ clavulanate or clindamycin in penicillin allergy.</td>
</tr>
<tr>
<td>Diabetic foot infections: Severe</td>
<td>cephalasine or amoxicillin/ clavulanate or clindamycin in penicillin allergy.</td>
</tr>
</tbody>
</table>

14
1.7 ALGORITHM DEVELOPED BY MATER DEI HOSPITAL (MDH) ANTIBIOTIC TEAM

The algorithm devised by MDH Antibiotic team in 2012 provides clinicians with multiple antibiotic treatment pathways which could be employed when treating different severities of lower limb wounds or ulcers.

As already discussed in section 1.1 limited information has been published which provides antibiotic algorithms or guidelines for the treatment of lower limb wounds or ulcers, whilst several publications provide information on the effect of specific antibiotics on wounds. This lack of available data limits this specific study in making comparisons with other studies employing a specific antibiotic rather than an algorithm or guideline.

The MDH Algorithm (Table 1.4), differentiates wounds following culture and sensitivity tests into these 4 subgroups. Furthermore, the algorithm describes which patients are considered as high risk for antibiotic resistance, fitting into one or more of these criteria:

- Resident in a nursing home
- Currently in hospital for ≥ 7 days
- Hospitalized in the previous 3 months
- MRSA positive in the past year
- On haemodialysis
- Wide spectrum antibiotic treatment in the previous month
Thus the treatment prescribed for low risk patients and high risk patients is different due to an increased probability of antibiotic resistance in high risk patients.

Table 1.4: The antibiotics used in the algorithm for lower limb wounds and ulcers developed by Mater Dei Hospital. (Guideline algorithm for the antibiotic treatment of common infectious diseases in the hospital setting, 2012)

<table>
<thead>
<tr>
<th>Infection subgroup</th>
<th>Treatment for non-high risk individual</th>
<th>Treatment for High risk Individuals</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colonisation</strong></td>
<td>Silver dressing</td>
<td>Silver dressing</td>
<td>5-7 days</td>
</tr>
<tr>
<td><strong>Non-severe Infection</strong></td>
<td>flucloxacillin</td>
<td>doxycycline</td>
<td>7-14 days</td>
</tr>
<tr>
<td>(if allergic to penicillin use of co-trimazole is advisable)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe infection</strong></td>
<td>clindamycin and ciprofloxacin</td>
<td>clindamycin and gentamicin</td>
<td>14-28 days</td>
</tr>
<tr>
<td><strong>Life threatening</strong></td>
<td>Continue as per sepsis algorithm</td>
<td>Continue as per sepsis algorithm</td>
<td>Continue as per sepsis algorithm</td>
</tr>
</tbody>
</table>
Furthermore, antibiotic treatment is also classified according to severity of the infection as described in Table 1.4. These classifications include (Table 1.2 and Figure 1.3):

**Non- Severe Infection:**
- No fever.
- Presence of: Pus or two or more signs of inflammation (erythema, warmth, pain, tenderness, induration).
- Infection is confined to skin or subcutaneous tissue.
- Cellulitis is less than 2cm surrounding wound.

**Severe Infection:**
- Fever ±.
- Lymphatic streaking.
- Deep tissue infection (involving subcutaneous tissue, fascia or tendon).
- Abscess.
- Cellulitis greater than 2 cm surrounding wound.

The algorithm developed by MDH antibiotic team is further described in Figure 1.3.
Figure 1.3: The whole algorithm as identified by the MDH antibiotic team (Guideline algorithm for the antibiotic treatment of common infectious diseases in the hospital setting, 2012).
1.8 **ANTIBIOTIC TREATMENT AND ANTIBIOTICS USED IN GUIDELINES**

As discussed in section 1.1 the Infection Control Team at MDH identified the need to introduce a wound algorithm in order to provide guidelines on the use of antibiotics regulating and aiding the practitioners' use of antibiotics. A pilot algorithm was released for feedback and was later recognised as the final version approved for use in 2012. Most of the published literature which describes the use of antibiotic in chronic wounds facilitated the completion of this algorithm and the review below gives an overview of the studies which aided MDH antibiotic team in developing the algorithm for infected lower limb wound or ulcers.

In a study conducted by Howell-Jones et al., 2006, the pattern of antibiotic prescription amongst data from the General Practice Morbidity Database (GPMD) for Wales was described. This identifies flucloxacillin as the antibiotic which was mostly prescribed for patients with chronic wounds (Figure 1.4. The MDH algorithm includes the use of flucloxacillin in non-severe infections. Prescription patterns for other antibiotics were identified in this study, some of which are used in the algorithm derived by the MDH antibiotic team (Howell-Jones et al., 2006).

Although Howell-Jones *et al.*, 2006, describe prescription patterns for antibiotic treatment in their study, the algorithm derived by MDH antibiotic team makes use of other antimicrobial treatment as described in Figure 1.3. Section 1.8 gives an overview of sensitivities and pharmacokinetics of these antibiotics.
Figure 1.4: A graph showing the prescription pattern in the General Practice Morbidity Database (GPDM) (Howell-Jones et al., 2006), where FLU (flucloxacillin), AMX (amoxicillin), AMC (co-amoxiclav), CEC (cefaclor), LEX (cefalexin), DOX (doxycycline), ERY (erythromycin), TMP (trimethoprim), MRZ (metronidazole), CIP (ciprofloxacin).

1.8.1 FLUCLOXACILLIN

This antibiotic is used in infections caused by streptococci, staphylococci spp., clostridia spp. and neisseria spp. Flucloxacillin is should not be used for infections against MRSA (Flavia et al., 2012). This antibiotic works by inhibiting the transpeptidation of the bacterial wall and hence producing a weakened peptidoglycan. Autolysin enzyme continues to weaken the bacterial wall resulting in osmotic lysis (Flavia et al., 2012). This antibiotics' peak serum levels achieved after 1 hr from absorption is 8.8mg/l for 250 mg dose and 14.5mg/l for 500mg dose. Absorption is increased if the antibiotic is taken prior to a meal. This would
increase the dose absorbed to 79%. It is excreted well by the kidneys and a part is excreted through the bile, but caution must be taken if administered to a patient with renal failure, as excretion in this case is slowed down. As described in the algorithm, flucloxacillin should not be used in individuals with a severe or life threatening infection (National Centre for Biotechnology Information. Compound Summary. Flucloxacillin).

The positive effect which is visible when administering flucloxacillin is noted in a study conducted by Sturup et al., 1987. They observed that when flucloxacillin was administered to six patients with chronic leg ulcers, at a dose of 1 g three times daily for 3 days given orally, the antibiotic dose in the serum was larger than the dose obtained from the exudates in the wound. However the dose noted in the exudates was higher than the Minimum Inhibitory Concentration dose. In this study it was also noted that the amount of \textit{Staphylococcus aureus} was reduced by 0.1% to that which was observed on commencement of the study (Sturup et al., 1987).

1.8.2 DOXYCYCLINE

Doxycycline is a tetracycline antibiotic whose activity is directed towards multiple organisms. In a review by Agwuh and MacGowan, 2006, it was described that bioavailability of doxycycline was > 80%, with absorption achieved mainly in the duodenum. The drug is 82%- 93% protein bound. Elimination takes place mainly through the kidneys and the biliary routes, although some hepatic metabolism has also been observed, as it has been found to be affected by rifampicin.
As described by Eleftheriadou et al., 2010, it is active against mild to moderate infections by *Staphylococcus aureus* but it is not effective in MRSA infections (Eleftheriadou et al., 2010). This can be further identified in an Italian study which was conducted on 1295 patients, which describe that doxycycline still shows sensitivity towards strains of *Staphylococcus aureus*. However, this study falls short describing its' effect on the MRSA strains of the pathogen (Tascini et al., 2011). In 2002, Bandyk described doxycycline as one of the antibiotics of choice when vascular surgeries were performed. It was chosen due to its effect on the inhibition of the matrix proteinases, and for their anti-inflammatory properties (Bandyk, 2002). This coincides with what Stechmiller et al., 2010 states. They argue that in a chronic wound, levels of pro-inflammatory cytokines and matrix metalloproteinases are elevated and these impair wound healing. Hence in this study they use topical doxycycline in order to improve chronic wound healing (Stechmiller et al., 2010). In a pre-clinical study, using rabbits Del Pozo et al., 2009, identified that *Staphylococcus epidermidis* bacterial load, significantly decreased with the use of doxycycline. However this study showed that low-amperage electrical current provided better results when bacterial load was compared between the two (Del Pozo et al., 2009).

1.8.3 CLINDAMYCIN

Clindamycin is an antibiotic which shows response towards aerobic Gram-positive cocci, anaerobic Gram-negative bacilli, anaerobic Gram-positive non-spore forming bacilli and anaerobic and microaerophilic Gram-positive cocci (Pfizer New Zealand Ltd, 2008). It works mainly by binding to the 50s ribosomal subunit of the offending bacteria. Interference will be achieved through this process and hence inhibiting the ability of protein synthesis.
Furthermore, changes in the bacterial cell wall would decrease the bacterial ability to adhere to host cells and hence decrease ability of bacteria to infect host (Johnson et al., 2013).

In a study by Bouazza et al, 2012 they used clindamycin to monitor it's pharmacokinetic properties in osteomyelitis, and it was chosen as it penetrates joints and bone. Moreover, it was discussed that doses need not be changed in individuals with renal or hepatic insufficiency. In this study, it was noted that clearance was affected by weight. Where, a 600mg dose three times daily was effective in individuals which were <75kg. In heavier individuals it was advised to increase the dose to 900mg every 8 hours. Moreover, it was also noted that rifampicin decreased serum concentrations of clindamycin, and although the sample number in this study was not big enough, it was still discussed that it could have resulted from an induction effect on the P450 cytochrome by rifampicin, which induces metabolism of clindamycin, hence the decreased serum concentrations, although further studies need to be conducted.

In a study conducted by Vidillac et al 2011, when clindamycin was compared to linopristine in combination with flopristine (NLX103) the latter showed better results against MRSA and Streptococcus pyogens invitro (Vidallac et al., 2011). In another article by La Plante et al., 2008, they argue that the use of clindamycin in community-associated MRSA provides good results, but some strains started becoming resistant to this antibiotic, and hence cause failure of treatment (La Plante et al., 2008).
1.8.4 GENTAMICIN

Gentamicin is another antibiotic which is recommended in the MDH algorithm. This antibiotic is made up of a complex of three aminoglycoside sulphates. Their mechanism of action is bactericidal. They bind directly to the RNA and inhibit the protein chain translation and miscoding (Yoshizawa et al., 1998). They also function by inhibiting the growth and replication of bacteria (National Center for Biotechnology Information. Compound Summary. Gentamicin, 2013).

In an article by Xuan et al (2003), they describe that in healthy individuals with a normal functional kidney, a daily dose of 7mg/kg would be enough to achieve satisfactory serum concentrations. However, they describe that in individuals, with hindered kidney function, serum concentrations monitoring is a requisite. Hence Hilmer et al, 2010 describe that the mean volume of distribution of gentamicin in the frail individuals is less than in the non-frail individuals by approximately 0.5. Clearance was also noted to be reduced in frail individuals. This could have resulted from the decreased renal function in these frail individuals as described in the article. Moreover, it was also highlighted by Sowinski et al, 2008, that individuals on haemodialysis, conventional doses are not efficient, and hence require larger doses pre-dialysis in order to achieve treatment.

Multiple studies produced positive results when gentamicin was used. One of which described a good sensitivity of gentamicin to multiple organisms found in diabetic foot ulcers, including Bacteroides fragilis, Pseudomonas spp and Clostridia spp (Ramani et al., 1991). Another more recent study, described the use of topical application of gentamicin-collagen sponge. Lipsky et al., 2012, describe that the treatment group showed improvement and cure in all 22
patients whilst in the non-treated group it was observed that only seven out of ten had a cured lesion (Lipsky et al., 2012). On the other hand, in another study conducted by Dissemond et al., 2004, it observed the sensitivity of multiple drugs for oxacillin-resistant *Staphylococcus aureus* (ORSA). Out of the 17 patients who were identified to be colonised with ORSA, only six were sensitive to gentamicin, whilst all ORSA were sensitive to vancomycin (Dissemond et al., 2004).

Alonge et al., 2002 also described the sensitivity of gentamicin. The difference in this study was, that here 47 isolates were identified and assessed, with *Staphylococcus aureus* being the most common. Results indicated that 30% of the total organisms cultivated showed sensitivity towards gentamicin (Alonge et al., 2002).

1.8.5 CIPROFLOXACIN

Ciprofloxacin is a fluoroquinolone antibiotic and it acts by inhibiting the enzyme responsible for DNA replication; topoisomerase enzyme (Fisher et al., 1989). Resistance to this antibiotic has been described, since gene mutations cause alterations in the DNA gyrase (Sanders 1988).

In a study conducted by Conil et al, 2008, it was described that in critically ill individuals with a mean age of 59±17 years, it was found that the volume of distribution of the drug was lower than in healthy individuals. It was also noted in this study, that plasma concentrations in critically ill patients is rarely obtained, and this could result from interindividual variability. Furthermore, this study highlights the importance of microbiological data, and states, that it is a requirement to identify the correct doses to be administered. This is of utmost importance,
as in a study by Gregoire et al, 2010, it has been observed, that subinhibitory concentrations result in a rapid growth of resistant microbes. This was observed with ciprofloxacin and *Pseudomonas aeruginosa*.

This antibiotic is effective against multiple bacteria which include *Pseudomonas aeruginosa*, *Staphylococcus epidemidis*, *Streptococcus pyogenes*, MRSA, *E.coli*, (National Center for Biotechnology Information. Compound Summary, 2013). Various studies have been recovered indicating the usage of ciprofloxacin antibiotic in the treatment of infections and diabetic foot infections. In a study by Silvanmailiappan et al., 2011, it was shown that out of the 15 antibiotics tested against strains of *Pseudomonas aeruginosa*, none of the antibiotics used showed 100% sensitivity, and only cefotaxime and ciprofloxacin showed the best results, with ciprofloxacin being the least sensitive out of the 2 (Silvanmailiappan et al., 2011).

This does not tally with what was described by Yoga et al., 2006, who describe that all *Pseudomonas aeroginosa* where sensitive to ciprofloxacin (Yoga et al., 2006). In a study conducted by Diamantopoulus et al., 1998, similar results were described. In this study, the combinatory effect of ciprofloxacin and clindamycin were found to have a positive effect on treatment of diabetic foot infections. In more than 75% of infections either improvement or resolution of the infection was noted (Diamantopoulus et al., 1998).

The antibiotics used in the algorithm for lower limb wounds or ulcers are summarised in Table 1.5. Their mode of action and their effectiveness against MRSA are also described in Table 1.5.
Table 1.5: A summary table showing the action of the antibiotics and their effect on MRSA

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Mode of action</th>
<th>Effective against MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flucloxacillin</td>
<td>Inhibits cell wall synthesis and cell division (Kohanski et al, 2010)</td>
<td>Not sensitive (Fuda et al, 2004)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>It inhibits matrix proteinases and has a positive effect on inflammation (Chopra, Roberts, 2001)</td>
<td>Effective, although resistance is being acquired. (Ernst, 2012)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Binds to 50s ribosomal subunit and interferes with protein synthesis (Smieja M, 1998)</td>
<td>Known resistance makes this antibiotic less efficient in treating MRSA</td>
</tr>
</tbody>
</table>
1.9 IDENTIFICATION OF ORGANISMS THROUGH THE USE OF WOUND SWABS AND CULTURE AND ANTIBIOTIC SENSITIVITY TESTS

As described in Section 1.1 in order to achieve the best results with the use of antibiotic treatment, it is important to identify appropriately the infecting organisms present, and which antibiotics are most advisable. In order to achieve this, various tests apart from observing the clinical signs of infection in a wound are available. These mainly if not entirely include culture and sensitivity tests.

Although there are studies which conclude that wound swabbing as an inaccurate technique for the identification of the real offending organisms in a wound, others argue that they still produce relevant results which could be used in the administration of antibiotics when an infection is present (Slater et al. 2004, Macias Hernandez et al. 2011, Levine and Evans 2001, Lim et al. 2006). Lim et al., 2006, described a distinction between wound swabbing and punch biopsy when compared and they advise on the use of punch biopsy for a more accurate result, (Lim et al., 2006). Mutluoglu et al., 2011 also described that in cases of diabetic foot ulcers, superficial wound swabs are not as reliable as deep tissue wound swabs, and provide inaccurate results which might lead to inappropriate administration of antibiotics (Mutluoglu et al. 2012). On the other hand, Macias Hernandez et al., 2011, Pellizzer et al., 2009 and Slater et al., 2004, all describe the importance of taking a wound swab and, although in these studies the biopsies provided a more accurate result with more organisms cultivated, they still obtained significant results for wound swabs. Thus implying their importance when infection is suspected and antibiotics are needed.
Slater et al, 2004, argues that if infection in wound was bone deep, deep tissue cultures obtained better results, but if no bone was involved, wound swab test provided reliable results. The proper technique when taking a wound swab for culture and sensitivity (C&S) testing is simple yet it is important that it is taken properly. This is so in order to minimize any risks of contamination and consequently increasing the reliability of the test. Two main methods for taking a wound swab have been identified. The Levine technique (were swab is rotated over 1 cm of the wound) and the Zig- Zag technique (were the swab is rotated in a zig- zag fashion on the wound), were compared in a study by Angel et al, 2011, and found that the Levine technique is more appropriate for an accurate wound swab, as when the two techniques were compared, the Levine technique identified significantly more organisms than the Zig- Zag technique.

1.9.1 RELIABILITY AND VALIDITY OF THE CULTURE AND SENSITIVITY WOUND SWABS

Reliability is a term used to confirm that the tool being used produces consistent results. A tool which is not reliable can never be validated (Keen, 2008)

Culture and sensitivity wound swabs, as described by Patten, 2011 provide a method to identify wound infection in a simple and convenient way, through a non-invasive method. However, there are studies which do question the reliability and validity of this method. One such study conducted by Mutluoglu et al, 2012, concluded that in diabetic foot ulcers, superficial wound swabs do not correlate well when compared to deep tissue biopsies.

Hence, the author concludes that results did not find wound swabs reliable when guiding the practitioners for antimicrobial treatment. On the other hand while Macias
Hernandes et al, 2011 described that a biopsy culture is the gold standard for identifying the microbiology of wounds, in their study they concluded that a swab culture is a practical method to determine the organisms present in a wound.

In fact, the authors obtained 0.85 sensitivity, 0.86 specificity, a positive predictive value of 0.98 and, a negative predictive value of 0.43. This is in accordance with the results obtained by Pellizzer et al, 2009 which showed that although, through experience, deep tissue culture results are more reliable and informative; wound swabbing and deep tissue cultures provided similar reliable results for monitoring of microbes in wounds. Furthermore, Gardner et al, 2006 stated that Levine's technique provided better results than wound exudate or Z-techniques (Gardner et al, 2006).
1.10 TOOL TO ASSESS VASCULAR SUPPLY: ANKLE BRACHIAL PRESSURE INDEX (ABPI)

The Ankle Brachial Pressure Index is a measure used to identify arterial insufficiency. This is a critical measure which must be used when assessing and treating lower limb wounds and ulcers (Worboys, 2006 and Ruff, 2003). This is done by obtaining a ratio for the resting brachial systolic pressure and the resting ankle systolic pressure. Having an ABPI between 1 and 1.3 would be within the normal range, indicating no arterial insufficiency (Table 1.6) (Worboys, 2006).

Table 1.6: A table indicating the values which could be obtained when performing the ABPI and their meaning.

<table>
<thead>
<tr>
<th>ABPI value</th>
<th>Clinical description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1.3</td>
<td>Normal</td>
</tr>
<tr>
<td>≥0.8</td>
<td>Indicative of slight arterial disease, but which does not hinder the arterial supply towards the lower limb</td>
</tr>
<tr>
<td>&lt;0.8</td>
<td>Indicative of arterial disease. In this case a vascular referral should be considered</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>Indicates extensive arterial disease. This value is indicative for urgent vascular referral</td>
</tr>
</tbody>
</table>

This is an important measure to include as part of the clinical investigations, since when gentamicin was administered to patients who were going to undergo a lower limb amputation, serum levels were greater than the levels of gentamicin obtained in the tissue.
(Zammit MC et al, 2011). This was also more evident in individuals with moderate to severe peripheral arterial disease. These results emphasise on the importance of good peripheral arterial circulation when treating foot wounds.

The EURODIALE study conducted by Prompers et al, 2007, in the European population, observed a significant difference in the effect of the combination of peripheral arterial disease and infection, on the rate of healing of a wound (Prompers et al, 2007). Moreover, it was noted, that the use of a hand held doppler provided a more accurate ABPI value. This was further supported by a study by Ena et al, 2011, which described that when an 8 MHZ hand held doppler was compared to an automated blood pressure measuring device, the hand held doppler provided better results.

1.10.1 Reliability and Validity of ABPI

As described by Keen 2008, basic guidelines are available which guide researchers performing ABPI. However, as yet no guidelines are available which would decrease any bias gained through confounding factors, such as exact cuff position (Keen, 2008). Confounding factors are described in Table 1.7. Caruana et al, 2005, described that a large variability was noted when the methodology of multiple studies where analysed on the conduction of ABPI measurement (Cao et al, 2001). In general, sensitivity and specificity of this tool could vary between 80%-95% and 95%-100%, respectively (Ena et al, 2011, Cao et al, 2001). Nevertheless these results may be hindered by diabetes. (Cao et al, 2001, Thompson et al, 2008) On the other hand Sangle et al, 2008 and Ena et al 2011, described that ABPI is a reliable and valid instrument with increased patient acceptability and it is also quick and easy to use. Advantages and disadvantages of the ABPI are described in Table 1.8.
Table 1.7: Variables which must be considered and accounted for prior to interpreting ABPI results (adapted from Keen, 2008).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Potential risks for not accounting for variable during ABPI assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cuff Position</td>
<td>Ankle systolic pressures may increase when cuff is not placed as low as possible in leg.</td>
</tr>
<tr>
<td>Patient Position</td>
<td>Hydrostatic pressure changes effect ABPI results.</td>
</tr>
<tr>
<td>Central systolic blood pressure</td>
<td>Hypertension may affect lowering of ABPI, and hypotension and treatment of hypertension may falsely raise ABPI.</td>
</tr>
<tr>
<td>Arterial calcification/atherosclerosis</td>
<td>If absolute pressures are not recorded, local arterial disease may not be recognised, therefore invalidating the ABPI, and risking tissue damage to under perfused areas when compression is applied.</td>
</tr>
<tr>
<td>Pre-test rest time/exercise</td>
<td>Hydrostatic pressure and raised central systolic pressure may affect the ABPI.</td>
</tr>
</tbody>
</table>
Table 1.8: Advantages and disadvantages of ABPI measurement (adapted from Cao et al, 2011).

<table>
<thead>
<tr>
<th><strong>Advantages</strong></th>
<th><strong>Disadvantages</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple, inexpensive, quick, widely applicable, cost-effective.</td>
<td>May be falsely elevated in patients with diabetes, renal insufficiency, and advanced age.</td>
</tr>
<tr>
<td>Sensitive in establishing or refuting Critical Limb Ischemia (CLI) diagnosis.</td>
<td>Indirect measure.</td>
</tr>
<tr>
<td>Useful to monitor efficacy of therapeutic interventions in CLI.</td>
<td>Does not provide localisation of disease.</td>
</tr>
<tr>
<td></td>
<td>Does not allow visualisation of artery lesion.</td>
</tr>
</tbody>
</table>
1.11 WOUND ASSESSMENT TOOL

The effectiveness of an antibiotic can be determined by examining the wound and the surrounding skin for improvement. This is carried out by using wound assessment tools. When assessing a wound, there are multiple factors which have to be assessed in order to categorize the wound. For this purpose, multiple wounds assessment/classification tools and wound charts have been produced and validated. Some tools are specific whilst others are generic. These include general wound assessment tools such as:

- National Wound Assessment form,
- The Wound Healing Continuum

and specific wound classification and assessment tools such as:

- The Wagner scale
- The Bates-Jensen Wound Assessment tool

For the purpose of this specific study, the Bates-Jensen wound assessment tool (BJWAT) was used. This wound assessment tool was developed for assessment of pressure wounds. However, even though it was primarily developed as a tool for pressure wounds, Romanelli et al 2007, described the Bates- Jensen Wound Assessment tool (see Appendix 2) as being the most validated and reliable tool which can be used for chronic wounds. This was also cited by the Integrated Client Care Project, 2009 which basing their information on a study conducted by Bolton et al 2004, this tool was purposely chosen in favour of other wound assessment tools.
1.11.1 RELIABILITY AND VALIDITY OF THE BATES-JANSEN WOUND ASSESSMENT TOOL

As described earlier in section 1.11, the Bates-Jensen Wound assessment tool (BJWAT) has been developed from the former Pressure Sore Status Tool (PSST). This tool has been tested for validity and reliability. For this tool the Content Validity Index has been the tool which was used to assess the validity of BJWAT. Validity has also been assessed in a research conducted by Bates-Jensen and McNees, 1995 which observed a good correlation between the BJWAT and PSST tool. Reliability has been confirmed through the experience of two experts in wounds who rated twenty ulcers on ten individuals using the PSST. Interater reliability was found to be high when ratings were taken at two intervals. Intrarater reliability was also found to be high when tested amongst nurses. (Cauble, 2010)

As described above, the Bates Jensen Wound Assessment Tool has been found to be reliable and valid. It was chosen in favour of other tools, as it measures various parameters of a wound which are indicative of infection. Furthermore it was chosen since, although it is primarily a pressure ulcer wound assessment tool, it was found to be reliable to use in other types of wounds as described in by Romanelli et al 2007, and Bolton et al, 2004.
1.12 FACTORS AFFECTING WOUND HEALING

There are multiple factors which might influence the rate of wound improvement. Holmes and Norman, 2008, as described in Table 1.9, describe multiple factors which might affect wound improvement. Various studies discuss solely these factors as limiting factors in wound healing.

Table 1.9: A diagram identifying factors which can adversely affect wound improvement. (Adapted from Holmes and Norman, 2008)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adverse local conditions at the wound site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrotic tissue</td>
<td>Fall in wound temperature</td>
</tr>
<tr>
<td>Fall in wound temperature</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Foreign body</td>
</tr>
<tr>
<td>Foreign body</td>
<td>Mechanical forces</td>
</tr>
<tr>
<td>Mechanical forces</td>
<td>Oedema</td>
</tr>
<tr>
<td>Oedema</td>
<td>Excess exudate</td>
</tr>
<tr>
<td>Excess exudate</td>
<td>Local hypoxia and oxygenation</td>
</tr>
<tr>
<td>Local hypoxia and oxygenation</td>
<td>Infection</td>
</tr>
<tr>
<td>Increasing age</td>
<td>Decreased epidermal cell replacement</td>
</tr>
<tr>
<td>Decreased epidermal cell replacement</td>
<td>Reduced inflammatory response to injury</td>
</tr>
<tr>
<td>Reduced inflammatory response to injury</td>
<td>Altered barrier functions of the skin</td>
</tr>
<tr>
<td>Altered barrier functions of the skin</td>
<td>Increased susceptibility to trauma</td>
</tr>
<tr>
<td>Increased susceptibility to trauma</td>
<td>Reduced sensory perception</td>
</tr>
<tr>
<td>Reduced sensory perception</td>
<td>Negative psychological factors</td>
</tr>
<tr>
<td>Negative body image resulting in problems with social relationships</td>
<td>Social isolation</td>
</tr>
<tr>
<td>Social isolation</td>
<td>Additional stress</td>
</tr>
<tr>
<td>Additional stress</td>
<td>Patients lack of belief in treatment</td>
</tr>
<tr>
<td>Patients lack of belief in treatment</td>
<td>Negative attitudes of staff towards</td>
</tr>
<tr>
<td>Negative attitudes of staff towards</td>
<td>Treatment and healing</td>
</tr>
<tr>
<td>Treatment and healing</td>
<td>Inappropriate wound management</td>
</tr>
<tr>
<td>Failure to identify and correct underlying cause</td>
<td>Application of inappropriate topical treatment</td>
</tr>
<tr>
<td>Application of inappropriate topical treatment</td>
<td>Poor wound dressing technique</td>
</tr>
<tr>
<td>Poor wound dressing technique</td>
<td>Adverse effects of other therapies</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>Cytotoxic drugs</td>
</tr>
<tr>
<td>Cytotoxic drugs</td>
<td>Prolonged high doses steroids</td>
</tr>
<tr>
<td>Prolonged high doses steroids</td>
<td>Miscellaneous drugs including anticoagulants, local anaesthetic alcohol and nicotine.</td>
</tr>
<tr>
<td>Miscellaneous drugs including anticoagulants, local anaesthetic alcohol and nicotine.</td>
<td>Pathophysiological factors</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Cardiovascular disorders</td>
</tr>
<tr>
<td>Cardiovascular disorders</td>
<td>Immune disorders</td>
</tr>
<tr>
<td>Immune disorders</td>
<td>Endocrine or metabolic disorders</td>
</tr>
<tr>
<td>Endocrine or metabolic disorders</td>
<td></td>
</tr>
</tbody>
</table>
1.12.1 Oxygenation and Revascularization

Guo and DiPietro, 2010 classify factors which can adversely affect wound improvement into two

- The systemic factors.
- The local factors.

These authors discuss the importance of oxygenation to the wound, hence implying that a good vascular supply to the wound is important since poor vascular perfusion to the wound results in a hypoxic wound, decreases healing and increases resistance to infection (Gottrup, 2004, Guo, DiPietro 2010). The authors suggest that oxygenation induces multiple healing processes such as angiogenesis, fibroblast proliferation, and collagen synthesis and wound contraction. The authors also described how important oxygenation is in superoxide production by polymorphonuclear leukocytes (which is a process where pathogens are oxidatively killed).

Guo and DiPietro described that in cases where oxygenation is not restored, healing is highly hindered. Hence it is important to restore proper oxygen, since as discussed by Gottrup, 2004, epidermal cells grow at an oxygen concentration of anything between 10%-50% levels to the wound for adequate wound healing, the values of which should be of about 30-50 mm Hg as described by Sheffield, 1988 (Tandara and Mustoe 2004, Guo, DiPietro 2010). Moreover, hypoxia results in multiple complications which might hinder wound healing as described in Figure 1.5.
Further to oxygenation and revascularization, other factors such as steroids, antiplatelet drugs, anaesthesia, and diabetes, might affect the rate of wound healing.
1.12.2 Steroids

Medications such as steroids are also found to hinder wound healing. In fact in a pre-clinical experimental study on mice, Alberti et al, 2012 described that administration of corticosteroids preoperative and postoperative of 10 mg/kg/day did not prove to impede wound healing when compared to controls. Although following the first week of treatment after the incision, the groups treated with either oral or intravenous corticosteroid, had a lower wound healing resistance, with no effect incurred by route of administration (Alberti, De Souza Vasconcellos, Petroianu 2012). On the other hand, in a review by Wang et al 2013, it is stated that treatment regimens and doses used of corticosteroids should be lower since otherwise they could lead to the inhibition of wound healing (Wang, Armstrong, Armstrong, 2013). What has been noted was that in individuals who had taken corticosteroids for a minimum of 30 days prior to surgery, presented increased rates of surgical wound site infections (Ismael et al 2011).

1.12.3 Antiplatelets and Analgesics

Aspirin has also been shown to retard the healing of a wound, A study by Santos and Monte-Alto-Costa, 2013, noted that wound healing was delayed in female mice only, thus confirming available information in literature, indicating sex, dependant responses to this drug. (Dos Santos, Monte-Alto-Costa 2013)

Moreover opioid analgesics were also found to cause a difference in the rate of wound healing. McGuire et al, 2006 identified that pain did result due to a difference in wound healing. Records of patients suffering from acute pain showed the worst the wound
improvement rate. It was thus being assumed; that the use of opioids on wounds might affect positively wound healing (Stein and Kuchler, 2013).

1.12.4 Non Insulin Dependent Diabetes Mellitus and Insulin Dependent Diabetes Mellitus

Diabetes is a common condition resulting in loss of tissue viability. This condition is very common amongst the Maltese population, where numbers amount to 33,260 as described by the International Diabetes Federation (IDF). This value amounts to a total of about 10% of the total Maltese population (Malta, 2014). Various studies evaluated whether; improved glycemic control, management of diabetes related risk factors and patient education, would result in improved micro and macro vascular complications, hence achieving better wound improvement (Gilliani et al., 2012). Such results lead to decreased diabetic complications which can be micro vascular, including retinopathy, nephropathy and neuropathy, or macro vascular including cerebrovascular disease and peripheral vascular disease. This was further described in a study by Alsaimary, 2008, where abnormally high glucose blood levels are responsible for damaging blood vessels resulting decreased blood supply to the area, causing slow healing ulcers which might become infected.
1.13 **AIMS AND OBJECTIVES OF THE STUDY**

As discussed in section 1.1, the algorithm provided by the Mater Dei Hospital (MDH) antibiotic team is currently being used to determine the treatment of lower limb infected wounds and ulcers.

Through this specific study, this algorithm will be validated through the assessment of the improvement in a wound through the use of a wound assessment tool, following culture and sensitivity swab tests and administration of antibiotics for infected lower limb wounds and ulcers as recommended by the algorithm. Thus the main aim is

- The validation of the Antimicrobial Treatment of Infected Lower Limb Wounds or Ulcers, designed by the Antibiotic team at MDH

The secondary objectives are:

- To determine the importance of proper antibiotic treatment and hence decreasing the risks for further complications for the patients
- To identify the need for proper cleansing of wounds prior to taking a wound swab in order to decrease the chances of contamination
- To determine compliance from practitioners with the algorithm
- To identify which organisms are more likely to be present in lower limb wounds in Malta
- To indicate the concordance of the wound swab results with the antibiotics administered.
- To explore the relationship between ABPI values and wound improvement.
• To identify other factors which might be implicated in wound improvement.

The methodology, with which these aims and objectives were addressed are described in the methodology chapter.
CHAPTER 2
METHODOLOGY
2.1 **RESEARCH DESIGN AND METHODS**

As described in Chapter 1, the aim of this specific study was to validate the recommended MDH algorithm for the treatment of infected lower limb wound and ulcers. This algorithm addresses the identification of the severity of lower limb infection and the administration of antibiotics as appropriate. It also divides the individuals to be treated in two groups.

- Those which are at high risk to antibiotic resistance.
- Those who are at low risk to antibiotic resistance.

This chapter will describe the study design, subject selection, inclusion and exclusion criteria, informed consent, ethical considerations, data collection methods and tools used in this dissertation.

2.2 **THE STUDY PROCEDURE**

The study procedure and methodology are outlined, in Figure 2.1. This explains the steps which were taken in order to conduct the study, following identification of participants. Other processes such as the procedure for taking an Ankle Brachial Pressure Index (ABPI) and the procedure for taking a wound swab are further described in detail in Figures 2.3, 2.4, Tables 2.1,2.2,2.3, and Section 2.8.
Identification of individuals appropriate for participation in this study was established according to the inclusion exclusion criteria. Individuals were identified from Surgical Out Patients at MDH

Patients were then asked for informed consent in their language of preference, either Maltese or English

Demographic data was collected

A swab for culture and sensitivity was taken pre-cleaning and post cleaning twice with saline

The Bates Jensen Wound Assessment Tool (BJWAT) was filled up by the researcher

Ankle Brachial Pressure Index (ABPI) was then carried out by the researcher

Patient was then given antibiotic treatment by the doctor, according to algorithm provided by MDH

Patients were then followed for two more visits. On each visit the BJWAT and demographic data were filled in

Following the completion of data collection, participants were then verbally thanked for their participation in the study

Figure 2.1: A flow diagram outlining the method used for data collection.
2.3 **Observational Non-Experimental Quantitative Study Design.**

For the purpose of this study an Observational, Non-Experimental Quantitative study design was employed. This study design was chosen since it allows the determination of a relationship between groups without the need for randomisation and manipulation of variables (LoBiondo- Wood, Haber, 2014). In order to conduct such research, quantitative or qualitative study designs can be chosen.

A quantitative study design was chosen in this specific study since; qualitative research does not generate numerical data and focuses mainly on the interpretation of documents (Greenhalgh, Taylor, 1997). Its objective is to generate clear patterns in groups of individuals in different social settings (California State University Long Beach, 2014). On the other hand quantitative research generates numerical data from scientifically approaches used for data collection. Such a methodology, will hence clarify the relationship between the cause and effect being studied, (Castellan, 2010). This process is achieved by accepting or rejecting the hypothesis formulated. Furthermore, quantitative data research uses tools in order to obtain the data needed, such as questionnaires, surveys, tests, and other different equipment (Castellan, 2010).

A non-experimental study design is usually chosen when a relationship is examined between groups. This does not necessitate randomisation of the sample population and no independent variables are manipulated by the researcher. What this study design necessitates is a clear and concise hypothesis which is based on literature available (LoBiondo- Wood,
Haber, 2014). This study design will provide us with descriptive results (Polit, Tatano Beck, 2012)

One disadvantage of a non-experimental study design includes the fact that other factors or variables may be different between the individuals in the population sample and hence will affect the results being observed by the researcher. Consequently non-experimental study designs are used when experimental study designs are not possible or not ethical to conduct. These studies are also important when the researcher needs to evaluate events in life as they occur at one point in time or in a long stretch of time (Polit, Tatano Beck, 2012).

2.4 STUDY DESIGN

Eighty subjects were recruited from either St. Vincent De Paul Residence for the elderly (SVPR) and, from Mater Dei Hospital (MDH) which is the main general hospital in Malta. The patients were identified at the Surgical Out Patients clinic and at Tissue Viability Clinic (TVU/TVC) at MDH or at SVPR. Those patients who presented with an infected lower limb wound or ulcers were identified as appropriate candidates for the study. They were then asked for informed consent in order to allow them to participate in this study.

2.4.1 SUBJECT SELECTION

As described by LoBiondo Wood and Haber (2006), inclusion and exclusion criteria are sets of norms which are established, and which are relevant to what the researcher is trying to identify within the research. These criteria are useful in decreasing as much as possible bias which can be introduced throughout the study and which would in turn limit the
strength of the study being conducted. These should be formulated rationally in order to decrease any "potential contamination" ((LoBiondo- Wood, Haber, 2014) of the subjects selected. These will in turn improve the accuracy and the ability to generalise the results being produced by the study. In this case, the inclusion and exclusion criteria have been formulated for the accessible population being studied (LoBiondo- Wood, Haber, 2014).

2.4.1.1 INCLUSION AND EXCLUSION CRITERIA OF PATIENTS

Patients had to meet the following formulated inclusion and exclusion criteria as stated below in order to be included in the study.

- Adults aged 18 years or over
- Be diagnosed with an infected wound. An infected wound will be diagnosed from the criteria described in the algorithm provided by the MDH antibiotic team. These were divided into two main categories as described in the algorithm.
  - Non- Severe Infection
  - Severe Infection
- Have a lesion present in the foot i.e. from the malleoli downward
- Individuals who provide informed consent

The exclusion criteria were

- Individuals with foot wounds, but which do not present with infection
- Individuals younger than 18 years
- Individuals who fail to provide informed consent
• Individuals who fall in the colonisation or in the life threatening groups of the algorithm. This is because, colonisation is not an infection, and no antibiotics are administered, and in the life threatening infections, the sepsis algorithm is then used.

2.5 ETHICAL CONSIDERATIONS

Prior to the study procedure described in section 2.3, a study protocol, informed consents, permissions from Data Protection Officer at MDH, Geriatric consultants, Vascular Consultants, Medical Superintendent at SVPR, TVU management staff and data collection tools where submitted first to the University of Malta Medical School Ethics Faculty board. This was accepted on 19th April 2013 (Appendix 3). Following the latter approval, the proposal was then submitted to University Ethics and Research Committee UREC for approval. Permission from UREC was then acknowledged on Thursday 9th May 2013 (Appendix 3).

In order to comply with data protection requirements, an index number was given to all participants in this study in order to protect the anonymity of the individuals. Patient's names and addresses were stored separately and used only if data had to be correlated to patients' index number if required. Once all data was collected, the names were removed from the data base.
2.6 DATA COLLECTION

Data collection was conducted over nine months, between the nine months of June 2013 and March 2014. Data was filled in two datasheets. One form consisted of the gathering of information regarding demographic data (Appendix 4). This form was used in order to gather demographic and other information belonging to the patient. Such information included gender, age, wound location, co-morbidities, ABPI value, culture and sensitivity wound swab results for pre-cleaning of wound and post cleaning of wound, classification of high or low risk of patient as described in algorithm and treatment plan for visit 1-3. The other form used was the BJWAT (Appendix 2) which identified if any improvement noted in the wound.

During the nine months, eighty patients who fulfilled the inclusion/exclusion criteria were invited to participate in the study through verbal and written consent as described in Appendix 5. The data was collected from St. Vincent De Paul Residence and Mater Dei Hospital surgical out-patients' clinic, and Tissue Viability Clinic (TVU). The patients were then classified according to categories satisfying the antimicrobial treatment of Infected Lower Limb Wounds or Ulcers, i.e.: high risk/severe, high risk/non-severe, low risk/severe, low risk/non-severe, according to the algorithm.
2.6.1 **Data Collection Tools**

ABPI measurement was performed on each patient by the same researcher in order to avoid any intraoperator variability. This procedure was carried out using Hadeco Bi-directional Doppler ES-100V3®. Prior to starting the ABPI measure, the patient was asked to rest in a flat position for a minimum of 10 minutes, as described in Tables 2.1, 2.2.
Table 2.1: A table identifying the method used to obtain the Brachial systolic pressure which will be used for ABPI.

<table>
<thead>
<tr>
<th>Step taken for identification of Brachial systolic pressure.</th>
<th>Figure illustrating the method used.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify Brachial pulse, following proper palpation.</td>
<td></td>
</tr>
<tr>
<td>Wrap cuff around upper arm above the elbow.</td>
<td>(Park et al, 2013)</td>
</tr>
<tr>
<td>Apply ultrasonic gel and position Doppler at 45° in the direction of the heart, adjusting the Doppler in order to obtain the best signal.</td>
<td></td>
</tr>
<tr>
<td>Inflate sphygmomanometer until no more sound is heard.</td>
<td></td>
</tr>
<tr>
<td>Deflate cuff slowly until the first audible sound is then heard.</td>
<td></td>
</tr>
<tr>
<td>That value is the systolic pressure.</td>
<td></td>
</tr>
</tbody>
</table>
Table 2.2: A table identifying the method used to obtain the Ankle systolic pressure which will be used for ABPI.

<table>
<thead>
<tr>
<th>Step taken for identification of Ankle systolic pressure.</th>
<th>Figure illustrating the method used.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Place sphygmomanometer just above the ankle.</td>
<td></td>
</tr>
<tr>
<td>Palpate Anterior Tibial Pulse (AT) Posterior Tibial Pulse (PT) Dorsalis Pedis (DP)</td>
<td>(Park et al, 2013)</td>
</tr>
<tr>
<td>Locate the signal with the Doppler following application of gel, and start inflating cuff.</td>
<td></td>
</tr>
<tr>
<td>Inflate until no more sound is heard.</td>
<td>(Park et al, 2013)</td>
</tr>
<tr>
<td>Start deflating slowly.</td>
<td></td>
</tr>
<tr>
<td>The first audible sound is then recorded.</td>
<td></td>
</tr>
<tr>
<td>Repeat for all three pulses and use the highest value obtained.</td>
<td>(Park et al, 2013)</td>
</tr>
</tbody>
</table>
Following the procedure described above in the above, the ABPI was calculated by using a simple formula described in Figure 2.2.

\[
\text{ABPI} = \frac{\text{Highest ankle systolic pressure}}{\text{Lowest brachial systolic pressure}}
\]

Figure 2.2: The formula used to calculate the ABPI.


2.6.2 CULTURE AND SENSITIVITY WOUND SWABS

A wound swab for culture and sensitivity was used in order to identify the organisms present and their sensitivities in the wound. The method which was used is described below.

This procedure is done by primarily cleaning the wound with normal saline or water vigorously twice for a few seconds each, prior to taking the test, as described by the algorithm. This is done in order to remove any traces of foreign matter such as debris, which might be present in the wound. The procedures employed for taking the wound swabs using the Levine technique are described in Figures 2.3, 2.4.
Sterile wound swab is opened, and sterile swab is removed from packet

Tube cover is removed from tube

Sterile swab was moistened with sterile 0.9\% saline to aid adherence of microbes

Swab is rotated on the wound over a 1 cm$^2$ area of the wound which does not include the wound edge or the peri-wound area of the wound.

Sufficient pressure was applied to the wound which aided in expressing fluid from the wound.

Figure 2.3: A flow diagram indicating the Levine technique which was used for obtaining the wound swab for culture and sensitivity (Angel et al, 2011)
Hands were cleansed with alcohol or soap and water prior to starting procedure.

Non-sterile gloves were worn.

Wound swab pre cleaning twice with saline was taken using the Levine technique described in Figure 2.3.

Wound was debrided as necessarily.

Wound was cleansed vigorously twice with saline for a few seconds each as described in the algorithm provided by MDH antibiotic team.

A second wound swab following cleaning was taken, using the Levine technique described in Figure 2.3.

Hands were washed appropriately, and the necessarily papers were filled. Wound swabs were then taken for culture and sensitivity testing at Mater Dei Hospital Pathology Laboratories.

Figure 2.4: A Figure indicating the methodology adopted for taking a wound swab (Patten, 2010).
The wound swabs collected were tested at Mater Dei Hospital Pathology lab. As a policy, if the lab cultures more than three microbes from a single wound swab, the result would conclude a mixed culture, and no identification of the microbes and their sensitivities would be available.
2.7 WOUND ALGORITHM

As described in the introduction, not all sections from the algorithm were used. Colonization and life threatening infections were not used, as colonization is not indicative of infection, and life threatening infections use another algorithm for treatment. Table 2.3 indicates the sections used from the algorithm, whilst Figure 2.5 indicates the full algorithm used by the MDH antibiotic team.

Table 2.3: A table indicating the two sections of the guidelines algorithm which were used in this study

<table>
<thead>
<tr>
<th>Infection subgroup</th>
<th>Treatment for non-high risk individual</th>
<th>Treatment for High risk Individuals</th>
<th>Duration of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-severe Infection</td>
<td>flucloxacillin (if allergic to penecillin use of Co-trimazole is advisable)</td>
<td>doxycycline</td>
<td>7-14 days</td>
</tr>
<tr>
<td>Severe infection</td>
<td>clindamycin and ciprofloxacin</td>
<td>clindaycin and gentamicin</td>
<td>14-28 days</td>
</tr>
</tbody>
</table>

The patients were divided into high risk patients by having either one or more of the criteria mentioned below.

- Residence in a nursing home pre-admission
- Currently in hospital for $\geq 7$ days
- Have been in hospital in the past 3 months
- Have contracted MRSA in the past year
• Are on haemodialysis
• Have been administered a wide-spectrum antibiotic in the past month

Furthermore patients were also divided according to severity of infection as mentioned below in Table 2.4:

Table 2.4: This table describes the criteria for identifying Non-Severe and Severe wounds.

<table>
<thead>
<tr>
<th>Non-Severe</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fever</td>
<td>Fever ±</td>
</tr>
<tr>
<td>Presence of: Pus or two or more signs of inflammation (erythema, warmth, pain, tenderness, induration)</td>
<td>Lymphatic streaking</td>
</tr>
<tr>
<td>Infection is confined to skin or subcutaneous tissue</td>
<td>Deep tissue infection (involving subcutaneous tissue, fascia or tendon)</td>
</tr>
<tr>
<td>Cellulitis is less than 2 cm surrounding wound</td>
<td>Abscess</td>
</tr>
<tr>
<td>No fever</td>
<td>Cellulitis greater than 2 cm surrounding wound</td>
</tr>
<tr>
<td>Presence of: Pus or two or more signs of inflammation (erythema, warmth, pain, tenderness, induration)</td>
<td></td>
</tr>
</tbody>
</table>
This Figure describes the whole algorithm as identified by the MDH antibiotic team (Guideline algorithm for the antibiotic treatment of common infectious diseases in the hospital setting, 2012).
2.8 DATA COLLECTION TOOLS

2.8.1 BATES- JENSEN WOUND ASSESSMENT TOOL (BJWAT)

The BJWAT was used for the collection of data regarding wound properties. This tool is available in English and did not require translation as it was only used by the researcher. This tool is used to measure multiple parameters of the wound which include (Bates- Jensen, 2001)

- **Size**: where the longest and widest part of the wound surface were multiplied. The result provided the size of the wound.

- **Depth**: This describes the depth and thickness of the wound. The tool also provides supplementary data on the wound depth as seen in Appendix 2.

- **Edges**: This uses the supplementary data provided by the tool in order to describe the wound edges as seen in Appendix 2.

- **Undermining**: This measures the area involved under the wound edges. This is done by inserting cotton tipped applicator and measuring how much it proceeds under the wound edge without the use of any excessive force, as shown in Figure 2.6.

![Figure 2.6: A diagram indicating the method used to measure undermining of the wound.](Wound Assessment, 2014).
Chapter 2 - Methodology

**Necrotic Tissue Type:** This uses the parameters suggested by the tool in order to identify the type of necrotic tissue present in the wound as described in Table 2.5.

Table 2.5: A table indicating the stages of necrotic tissue type.

<table>
<thead>
<tr>
<th>Figure</th>
<th>Wound stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.jpg" alt="Image" /></td>
<td>No visible necrotic tissue is visible (Stokowski, 2010)</td>
</tr>
<tr>
<td><img src="image2.jpg" alt="Image" /></td>
<td>White/grey non-viable tissue and non adherent yellow slough (Gardner, 2013)</td>
</tr>
<tr>
<td><img src="image3.jpg" alt="Image" /></td>
<td>Loosely adherent yellow slough (Wound Assessment, 2014)</td>
</tr>
<tr>
<td><img src="image4.jpg" alt="Image" /></td>
<td>Loosely adherent soft black eschar (necrotic tissue) (Wound Assessment, 2014)</td>
</tr>
<tr>
<td><img src="image5.jpg" alt="Image" /></td>
<td>Firmly adherent hard black eschar (necrotic tissue) (Wound Assessment, 2014)</td>
</tr>
</tbody>
</table>
**Necrotic Tissue amount:** This uses a transparent metric measure to calculate the percentage of necrotic tissue present in the wound.

**Exudate Type:** Following proper cleaning of the wound, due to prior use of wound dressings which may react with the wound, the exudate type is described according to the criteria advised by the tool.

**Exudate Amount:** This measures the amount of wound exudate by the use of a transparent metric guide which measures the percentage of wound exudate present in the dressing.

**Skin colour surrounding wound:** This describes the colour of the tissue in the 4 cm parameter surrounding the wound.

**Peripheral Tissue Oedema and Induration:** This assesses the 4 cm tissue parameter surrounding the wound oedema is assessed by pressing the tissues for 5 seconds; if it remains indented that is non-pitting oedema. Induration is assessed by pinching gently the tissues; induration will be present when the tissues will not be able to be pinched.

**Granulation tissue:** This measures the area of the granulation tissue by the use of a transparent metric guide to measure the percentage of area covered with the growth of small blood vessels and connective tissue.

**Epithelisation:** This is the process of resurfacing and appears as red or pink skin. This is measured by the use of a transparent metric guide. The percentage of the wound filled with epithelial tissue is then measured.

For each parameter of the BJWAT, a value from 1-5 is given. The results from all parameters are added and values obtained indicated in Table 2.6.
Table 2.6: A table indicating the rating value obtained in the BJWAT and the indication of wound severity

<table>
<thead>
<tr>
<th>Value obtained</th>
<th>Indication of Wound Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-20</td>
<td>Minimal severity</td>
</tr>
<tr>
<td>21-30</td>
<td>Mild severity</td>
</tr>
<tr>
<td>31-40</td>
<td>Moderate severity</td>
</tr>
<tr>
<td>41-65</td>
<td>Extreme severity</td>
</tr>
</tbody>
</table>

(Sussman, Bates-Jensen, 2007)

The values from each visit were then assessed by the practitioner in order to observe if severity of wound decreased.

2.8.2 **ANKLE BRACHIAL PRESSURE INDEX METHODOLOGY**

Proper ABPI assessment is of utmost importance as this will indicate the severity of arterial disease in an individual. This procedure determined the probability of wound healing since one of the factors which determines wound healing is a satisfactory blood supply to the wound (Ruff, 2003, Sangle et al, 2008). This procedure makes use of:

- A couch or bed (to allow individual to be in a complete rested/ supine position).
- A hand held Doppler with an 8mHZ probe.
- Ultrasound transducer gel and a sphygmomanometer and cuff in order to be able to compress the arteries (Ruff, 2003).
In a study conducted by Ena et al, 2011, it has been determined that the use of a hand held Doppler provides a more accurate result than when using an automated blood pressure measuring device. Hence as described above an 8MHZ probe was used (Ena et al, 2011).

2.9 SAMPLING

For the purpose of this study non-probability sampling was employed, specifically purposive sampling. This type of sampling was used, since it allows the selection of the subjects as participants in the study according to the criteria set by the researcher. The population chosen would be one which is typical for the population under consideration (LoBiondo-Wood, Haber, 2014).

2.10 INFORMED CONSENT

Participants taking part in this study were invited verbally and in writing in order to participate in this dissertation. This was done in the languages the participant felt most comfortable with (English or Maltese). Subjects were asked to read the information sheet supplied in both Maltese and English language (Appendix 5). A full verbal explanation was given to the individuals participating in the study. When the individual was not able to provide an informed consent the next of kin available (e.g. wife/husband, son/daughter) was asked to provide informed consent following reading and properly understanding what the research involved. When no relative was available to provide informed consent, the medical consultant was asked to provide consent. The purpose of this study was fully explained to the
participants and they were given time to ask questions. Any queries raised were answered. Upon providing a verbal consent the participants were asked to sign a consent form (Appendix 5). The consent form and the information sheet specified that the participants should they wished to withdraw from the study, were free to do so at their own will and at any time they felt that they wanted to withdraw. Participants were guaranteed that their name would not be made identifiable when the results of this study were published, and also the participants were guaranteed that confidentiality would be kept throughout the data collection and also after the results were made public. All data collected remained strictly confidential.

2.11 METHODOLOGY FOR LITERATURE SEARCH

The literature search for this dissertation has been conducted through identification of articles from PubMed and other sources including Science Direct and google search engine. The literature search was conducted in the sixteen months of April 2013 to August 2014. The keywords which have been used to identify literature from these sources include:

- Wound Infection
- Wound infection and characteristics of wound infection/ bacterial flora/Antibiotic treatment
- Lower limb wounds and antibiotic treatment
- Antibiotic resistance/ Antibiotic resistance and lower limb wound infections
- WHO and antibiotic resistance
- Antibiotic use in Malta
International/ foreign antibiotic guidelines

Colonisation/ Colonisation and infection

Difference between colonisation and infection

Flucloxacillin/ Doxycycline/ Clindamycin/ Gentamycin/ Ciprofloxacin/ Pharmacokinetics/ Pharmacodynamics

Flucloxacillin/ Doxycyclin/ Clindamycin/Gentamycin/Ciprofloxacin and wound improvement/ lower limb wounds

MRSA infection and antibiotic treatment

Reliability and Validity of C&S/ ABPI/ BJWAT

ABPI/ C&S/ wound BIOPSIES method

BJWAT/ wound assessment tools

Factors effecting wound healing

Asprin/ pain killers/ warfarin/ antiplatelet/ analgesics/ steroid/ oxygenation/ IDDM/ NIDDM and wound improvement

Number of Diabetics in Malta

Glycemic control and wound infection

These keyword provided a skeleton for collection of data used for the literature review and methodology chapters.
2.12 **STATISTICAL ANALYSIS**

Statistical analysis was then carried out on the data collected from the participants (Appendix 7). All the data was recorded on a spread sheet and analysed using Microsoft Excel and **SPSS®** version 22.

Statistical analyse was used to determine the validation of the use of MDH Antibiotic algorithm for the treatment of lower limb wound and ulcers. The data was tested for normal distribution. The Shapiro Wilk test was used, since it is more powerful than the Kolmogorov-Smirnov test. Analysis of the data collected is described in Chapter Three (Ghasemi, Zahediasl, 2012).
CHAPTER 3
RESULTS
3.1 **FOREWORD**

As already discussed in Chapter 1, this study was used to identify whether wound improvement is possible when the MDH algorithm for the treatment of infected lower limb wounds or ulcers is used. In this section, the results collected from this study are described. These include:

- Difference in wound improvement with antibiotic therapy according to algorithm.
- Compliance with algorithm concordance with algorithm difference in wound swab culture and sensitivity results between pre-cleaning and post-cleaning.
- Other factors which might have affected the rate of wound improvement.

Statistical tests were conducted by SPSS ® version 22, and Microsoft Excel.

3.2 **DEMOGRAPHIC DATA**

Demographic data collected was analysed. The majority of the participants were males (51: 29). The age for the participants in this study ranged from 50 to 94, and when divided into age group categories the results were as described in table follow in Table 3.1. The largest number was in the 71-80 years age group category.
Table 3.1: The age groups and the number of participants in each age group.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 years or less</td>
<td>16</td>
</tr>
<tr>
<td>61-70 years</td>
<td>20</td>
</tr>
<tr>
<td>71-80 years</td>
<td>25</td>
</tr>
<tr>
<td>81 years or more</td>
<td>19</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>

As illustrated in Figure 3.1, when the ABPI was assessed, the majority of individuals had a decreased ABPI, with the highest percentage ranging being between the values of 0.5-0.8.

Figure 3.1: A bar graph indicating the number of participants according to the Ankle Brachial Pressure Index (ABPI), where calcification indicates a value higher than 1.3.
Nine individuals were non-diabetic, 38 individuals were diabetics and on insulin treatment and 33 were on anti-diabetic medication. Results are described in Table 3.2.

Table 3.2: The number of participants being Diabetic on insulin, or on oral anti-diabetic agents, or diet, and Non-Diabetics.

<table>
<thead>
<tr>
<th>Diabetes Type</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDDM</td>
<td>38</td>
</tr>
<tr>
<td>NIDDM</td>
<td>33</td>
</tr>
<tr>
<td>Non-Diabetic</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>

The 80 individuals were divided as described by the algorithm into low risk and high risk, and non-severe and severe infection. Results are described in Table 3.3 below.

Table 3.3: A table indicating the number of participants being High/ Low Risk, Severe/ Non-Severe.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Infection</th>
<th>Low Risk</th>
<th>High Risk</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Severe</td>
<td>9</td>
<td>12</td>
<td>21</td>
<td>59</td>
</tr>
<tr>
<td>Severe</td>
<td>38</td>
<td>21</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47</strong></td>
<td><strong>33</strong></td>
<td><strong>80</strong></td>
<td></td>
</tr>
</tbody>
</table>
3.3 Patient's Characteristics

The patients were divided in various categories which have been described in Figure 3.2.

Figure 3.2: Represents a flow diagram indicating a summary of how the patients were divided. Where NS/HR; Non-Severe wound infection (WI) / High Risk, NS/LR; Non-Severe (WI)/ Low Risk, HR/S; High Risk/ Severe (WI), LR/S; Low risk/ Severe (WI), Y; concordant

All participants showed improvement except for one participant whose wound improvement remained static.
with wound swab sensitivity result post-clean, N; no concordance with wound swab sensitivity result post-clean, P; partial concordance with wound swab sensitivity result post-clean, N/A; No information given with regard to concordance with wound swab sensitivity result post-clean.

3.4 WOUND IMPROVEMENT WITH REGARDS TO THE ALGORITHM

As already described in Section 2.11 in the methodology chapter, the Shapiro Wilk test was used to identify normality of the data, since it is more powerful than the Kolmogorov-Smirnov test (Ghasemi, Zahediasl, 2012). The results were found to be normally distributed, hence parametric tests were used to analyse the data.

The Freidman's Test was used to compare mean rating scores for a particular parameter, between the first, second and third visit (Hinton et al, 2014). The Null Hypothesis specifies that mean rating scores are comparable and are acceptable if the \( p \)-value exceeds the 0.05 level of significance. The alternate Hypothesis specifies that the mean rating score differs significantly and is accepted if \( p \)-value is lower than the 0.05 criterion.

Table 3.4 shows the mean wound improvement in all parameters which are assessed by the Bates Jensen Wound Assessment Tool, and describes significant result that reflects wound improvement visible in all parameters of the tool in all the wounds of the participants.
Table 3.4: Indicates the parameters of the BJWAT, the mean wound improvement and the \( p \)-value obtained for all participants.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>1.68</td>
<td>1.58</td>
<td>1.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depth</td>
<td>4.14</td>
<td>3.09</td>
<td>2.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Edges</td>
<td>3.81</td>
<td>2.75</td>
<td>2.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Undermining</td>
<td>2.26</td>
<td>1.30</td>
<td>1.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Necrotic Tissue Type</td>
<td>2.56</td>
<td>1.58</td>
<td>1.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Necrotic Tissue Amount</td>
<td>2.91</td>
<td>1.65</td>
<td>1.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exudate Type</td>
<td>3.15</td>
<td>2.45</td>
<td>2.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exudate Amount</td>
<td>3.24</td>
<td>2.75</td>
<td>2.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skin colour Surrounding wound</td>
<td>3.51</td>
<td>2.65</td>
<td>2.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peripheral Tissue Oedema</td>
<td>2.98</td>
<td>2.21</td>
<td>1.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peripheral Tissue Induration</td>
<td>2.20</td>
<td>1.61</td>
<td>1.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Granulation Tissue</td>
<td>4.60</td>
<td>3.55</td>
<td>2.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epithelisation</td>
<td>4.91</td>
<td>4.30</td>
<td>3.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>41.95</td>
<td>31.46</td>
<td>25.45</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Chapter 3 - Results

The one-way ANOVA is a test which was used to compare mean reduction in scores between several (two or more) independent groups (De Muth, 2014).

As described in Table 3.5, the lower limb and wound algorithm is validated, as the result obtained using ANOVA testing for compliance (adherence or non adherence to the algorithm by practitioners) resulted in a significant \( p\)-value, hence indicating that the Alternative hypothesis is accepted, showing that there is a significant difference between compliance and non-compliance to the algorithm in the rate of wound improvement.

Regression analysis results indicate that compliance with algorithm was a significant factor, with a \( p\)-value of 0.0102.

Table 3.5: A table indicating the wound improvement (mean reduction in BJWAT score) with compliance to algorithm.

<table>
<thead>
<tr>
<th></th>
<th>Number of Participants</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Standard Error</th>
<th>95% Confidence Interval for Mean</th>
<th>( p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>Non compliant</td>
<td>33</td>
<td>13.73</td>
<td>7.298</td>
<td>1.270</td>
<td>11.14</td>
<td>16.32</td>
</tr>
<tr>
<td>Compliant</td>
<td>47</td>
<td>18.45</td>
<td>8.185</td>
<td>1.194</td>
<td>16.04</td>
<td>20.85</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>16.50</td>
<td>8.127</td>
<td>0.909</td>
<td>14.69</td>
<td>18.31</td>
</tr>
</tbody>
</table>

Tables 3.6 and 3.7 describe that risk to antibiotic resistance, and severity do not affect the rate of wound improvement. However, the mean values in Tables 3.6 and 3.7 indicate that there is a difference in the results when risk and severity are assessed.
Table 3.6: A table indicating the mean improvement in wound (reduction in BJWAT score) with risk for antibiotic resistance.

<table>
<thead>
<tr>
<th>Number of Participants</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Standard Error</th>
<th>95% Confidence Interval for Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td><strong>Low Risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>16.00</td>
<td>8.151</td>
<td>1.322</td>
<td>16.04</td>
<td>20.85</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>16.95</td>
<td>8.178</td>
<td>1.262</td>
<td>13.32</td>
<td>18.68</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>80</td>
<td>16.50</td>
<td>8.127</td>
<td>14.69</td>
<td>18.31</td>
</tr>
</tbody>
</table>

Table 3.7: A table indicating the mean wound improvement (reduction in BJWAT score) with severity of wound infection.

<table>
<thead>
<tr>
<th>Number of Participants</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Standard Error</th>
<th>95% Confidence Interval for Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>59</td>
<td>17.49</td>
<td>7.682</td>
<td>1.000</td>
<td>15.49</td>
<td>19.49</td>
</tr>
<tr>
<td><strong>Non-Severe</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>13.71</td>
<td>8.872</td>
<td>1.936</td>
<td>9.68</td>
<td>17.75</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>80</td>
<td>16.50</td>
<td>8.127</td>
<td>14.69</td>
<td>18.31</td>
</tr>
</tbody>
</table>

On the other hand, Table 3.8 assesses both risk and severity simultaneously, and no significant difference is noted, however mean differences indicate that individuals with severe infection, who were either high risk or low risk, did obtain better results than the other groups. Since $p$-value (0.214) is higher than 0.05 level of significance, this indicates that the mean scores for different severity/risk categories vary marginally. Hence it cannot be generalized
that specific severity/risk categories will provide a significant increased improvement over another, as described in the Post-Hoc tests in Table 3.9. This lack of significance may be partly attributed to the small sample size. It is possible that with a larger sample, the difference between the means in wound improvement may become significant.

Table 3.8: A table indicating the mean wound improvement (reduction in BJWAT) with severity of wound and with antibiotic resistance risk.

<table>
<thead>
<tr>
<th>Number of Participants</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Standard Error</th>
<th>95% Confidence Interval for Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>HR/S</td>
<td>31</td>
<td>17.74</td>
<td>8.066</td>
<td>1.449</td>
</tr>
<tr>
<td>LR/S</td>
<td>28</td>
<td>17.21</td>
<td>7.370</td>
<td>1.393</td>
</tr>
<tr>
<td>NS/LR</td>
<td>10</td>
<td>12.60</td>
<td>9.629</td>
<td>3.045</td>
</tr>
<tr>
<td>HR/NS</td>
<td>11</td>
<td>14.73</td>
<td>8.463</td>
<td>2.552</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>16.50</td>
<td>8.127</td>
<td>0.909</td>
</tr>
</tbody>
</table>

Table 3.9: Post-Hoc tests for wound improvement with risk for antibiotic resistance and severity of wound.

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Difference</th>
<th>Standard Error</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR/S - LR/S</td>
<td>0.528</td>
<td>2.108</td>
<td>0.994</td>
</tr>
<tr>
<td>HR/S -NS/LR</td>
<td>5.142</td>
<td>2.941</td>
<td>0.306</td>
</tr>
<tr>
<td>HR/S - HR/NS</td>
<td>3.015</td>
<td>2.838</td>
<td>0.713</td>
</tr>
<tr>
<td>LR/S - NS/LR</td>
<td>4.614</td>
<td>2.979</td>
<td>0.414</td>
</tr>
<tr>
<td>LR/S - HR/NS</td>
<td>2.487</td>
<td>2.877</td>
<td>0.823</td>
</tr>
<tr>
<td>NS/LR - HR/NS</td>
<td>2.127</td>
<td>3.533</td>
<td>0.931</td>
</tr>
</tbody>
</table>
General linear model tests as described in Table 3.10, also further emphasise the results obtained earlier in Tables 3.6 and 3.7, where severity of wound infection, and risk for antibiotic resistance are found not to have influenced improvement of wound infection, although the individuals who presented with a severe wound infection were found to do better in the mean wound improvement score than those who presented with a non severe infection, by a score of 2.87. Furthermore, individuals who were high risk for antibiotic resistance, have achieved a higher wound improvement than those who were identified as low risk for antibiotic resistance, by a mean value of 0.891.

Table 3.10: A table indicating the general linear model result for severity of wound and risk for antibiotic resistance

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Standard Error</th>
<th>T</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>11.903</td>
<td>1.865</td>
<td>6.381</td>
<td>0.000</td>
</tr>
<tr>
<td>Severity: severe</td>
<td>2.867</td>
<td>2.015</td>
<td>1.422</td>
<td>0.159</td>
</tr>
<tr>
<td>Severity: Non-severe</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Risk: High Risk</td>
<td>0.891</td>
<td>2.784</td>
<td>0.320</td>
<td>0.750</td>
</tr>
<tr>
<td>Risk: Low Risk</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
3.4.1 Compliance with wound algorithm as described by the Mater Dei Antibiotic Team

Compliance with the algorithm was not observed in all individuals participating in this study. In fact Table 3.11, describes the number of individuals who were compliant or non-compliant with the algorithm.

Table 3.11: A table indicating the individuals who were compliant or non-compliant with the algorithm with regards to the severity and risk parameters.

<table>
<thead>
<tr>
<th></th>
<th>Compliant</th>
<th>Non-compliant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR/S</td>
<td>16</td>
<td>15</td>
<td>31</td>
</tr>
<tr>
<td>LR/S</td>
<td>22</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>HR/NS</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>LR/NS</td>
<td>2</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47</strong></td>
<td><strong>33</strong></td>
<td><strong>80</strong></td>
</tr>
</tbody>
</table>

Furthermore, Table 3.12 indicates the mean wound improvement when the patients were stratified according to risk for antibiotic resistance and severity for wound infection and compliance simultaneously. The table indicates that those who were high risk and compliant achieved the best result in wound improvement, whilst it can also be observed that in all groups, except for the low risk and severe group, all individuals who were compliant with the
wound algorithm obtained better results than those who were not compliant. In fact when a chi- squared test was performed as described in Table 3.13, a significant $p$-value of 0.009 was obtained, indicating that compliance was significant when risk and severity were evaluated.

Table 3.12: A table indicating the mean wound improvement in those patients who were compliant or non-compliant according to the wound severity and risk for antibiotic resistance.

<table>
<thead>
<tr>
<th>Risk/Severity</th>
<th>Compliance</th>
<th>Mean wound improvement</th>
<th>No of individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR/S</td>
<td>Yes</td>
<td>21.13</td>
<td>16</td>
</tr>
<tr>
<td>HR/S</td>
<td>No</td>
<td>14.13</td>
<td>15</td>
</tr>
<tr>
<td>LR/S</td>
<td>Yes</td>
<td>15.36</td>
<td>22</td>
</tr>
<tr>
<td>LR/S</td>
<td>No</td>
<td>15.67</td>
<td>6</td>
</tr>
<tr>
<td>LR/NS</td>
<td>Yes</td>
<td>17.5</td>
<td>2</td>
</tr>
<tr>
<td>LR/NS</td>
<td>No</td>
<td>11.38</td>
<td>8</td>
</tr>
<tr>
<td>HR/NS</td>
<td>Yes</td>
<td>15.14</td>
<td>7</td>
</tr>
<tr>
<td>HR/NS</td>
<td>No</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>
Table 3.13: A table indicating the effects of compliance on risk and severity parameters.

<table>
<thead>
<tr>
<th>Severity / Risk</th>
<th>HR/S</th>
<th>LR/S</th>
<th>NS/LR</th>
<th>HR/NS</th>
<th>Non-compliant</th>
<th>Compliant</th>
<th>Total number of individuals according to severity and risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15</td>
<td>6</td>
<td>8</td>
<td>4</td>
<td>16</td>
<td>22</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>22</td>
<td>2</td>
<td>7</td>
<td>28</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>28</td>
<td>10</td>
<td>11</td>
<td>80</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( \chi^2: 11.495 \) \text{ } p-value: 0.009

However when both parameters are assessed on their own, severity obtained a significant \( p\)-value, whilst risk did not hence further supporting the results obtained above, indicating that compliance and severity are complementary, as described in Table 3.14 and 3.15, whilst risk for antibiotic resistance is not a strong predictive parameter.
Table 3.14: A table indicating the significant difference between compliance and severity of wound parameters.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Non-compliant</th>
<th>Compliant</th>
<th>Total number of individuals according to severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>21</td>
<td>38</td>
<td>59</td>
</tr>
<tr>
<td>Non-severe</td>
<td>12</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>47</td>
<td>80</td>
</tr>
</tbody>
</table>

$\chi^2: 2.968 \ p-value: 0.05$

Table 3.15: A table indicating the significant difference between compliance and risk to antibiotic resistance parameters.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Non-compliant</th>
<th>Compliant</th>
<th>Total number of individuals according to risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>14</td>
<td>24</td>
<td>38</td>
</tr>
<tr>
<td>High risk</td>
<td>19</td>
<td>23</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>47</td>
<td>80</td>
</tr>
</tbody>
</table>

$\chi^2: 0.580 \ p-value: 0.446$
Chapter 3 - Results

The general linear model in Table 3.16, shows that the only factor which significantly influences the wound improvement results is compliance where a \textit{p-value} of 0.02 was obtained, this is in agreement with table 3.5. Whilst the severity/ risk factor does not influence significantly the wound improvement, but as described in the means, a difference is observed in the mean wound improvement, where those patients who were HR/NS, LR/S, HR/S obtained better results than participants who were NS/LR.

Table 3.16: A table indicating the general linear model analysis result for compliance and severity/ risk parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Standard Error</th>
<th>T</th>
<th>\textit{p-value}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>11.809</td>
<td>2.665</td>
<td>4.431</td>
<td>0.000</td>
</tr>
<tr>
<td>Compliance: Yes</td>
<td>4.585</td>
<td>1.926</td>
<td>2.380</td>
<td>0.020</td>
</tr>
<tr>
<td>Compliance: No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HR/S</td>
<td>3.566</td>
<td>2.764</td>
<td>1.290</td>
<td>0.201</td>
</tr>
<tr>
<td>LR/S</td>
<td>1.802</td>
<td>2.808</td>
<td>0.642</td>
<td>0.523</td>
</tr>
<tr>
<td>HR/NS</td>
<td>0.126</td>
<td>3.531</td>
<td>0.036</td>
<td>0.972</td>
</tr>
<tr>
<td>NS/LR</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

85
3.5 RESULTS RELATED TO WOUND SWAB TESTING

One of the secondary objectives of this study was to determine the importance of cleaning twice with saline prior to taking a wound swab, as advised by the Mater Dei Antibiotic team. The results obtained are described in this section. Figure 3.3 indicates the number of organisms identified pre-clean and post clean.

![Bar graph indicating the number of organisms identified from wound swabs pre cleaning twice with saline, and post cleaning twice with saline as advised by the guidelines. (Three participants are included in this table, which were not included in the study population as they presented with no organisms in the post clean wound swab result, hence indicating no infection).]
Chapter 3 - Results

Furthermore, the results obtained indicated that following cleaning twice with saline, 54 individuals obtained a decreased number of organisms as compared to the wound result from the pre-cleaning results. Twenty six individuals out of eighty obtained the same results in pre-clean wound swabs, and in post-cleaning wound swabs, that is no difference in number of organisms reported from pre-clean of wound swab to post-clean.

Appendix 6 describes the severity and risk the difference in the number of organisms from pre-clean to post-cleaning, and the improvement of the wound from visit 1 to visit 3 of the study.

The chi squared test was used to assess the association between the number of microbes prior to cleaning, and post-cleaning of the wound twice with saline, as advised by the MDH antibiotic team. The Null hypothesis specifies that there was no change in the number of microbes between pre-cleaning and post-cleaning, and is accepted if the $p$-value exceeds the 0.05 level of significance. The Alternate hypothesis specified that there was a significant reduction in the number of microbes between the pre-cleaning and the post-cleaning of the wound, swab results.

As described in Table 3.17, the total number of microbes between the two swabs differed significantly, indicating that cleaning the wound does produce a different result.
Table 3.17: A table indicating the difference in the total number of organisms pre- cleaning of the wound and post cleaning of the wound.

<table>
<thead>
<tr>
<th>Number of organisms</th>
<th>Highly mixed</th>
<th>1 microbe</th>
<th>2 microbes</th>
<th>3 microbes</th>
<th>Total number of individuals according to number of organisms post-clean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Highly mixed Count</td>
<td>0</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>1 microbe Count</td>
<td>0</td>
<td>11</td>
<td>9</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>2 microbes Count</td>
<td>0</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>3 microbes Count</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 34.884, p\text{-value:} < 0.001 \]

As described in Table 3.18 the chi squared test found a significant difference when the risk for antibiotic resistance was compared with the number of organisms present post-cleaning of the wound. However this was not the case when the risk for antibiotic resistance was evaluated for the number of organisms pre- cleaning of the wound, where a \( p\text{-value} \) of...
0.113 was obtained. Furthermore, wound severity was also not indicative as a factor affecting the number of organisms pre-cleaning and post-cleaning, where the \( p \)-values obtained were 0.084 and 0.284 respectively. Whilst when the two parameters are assessed simultaneously, no statistical significance was observed, with a \( p \)-value of 0.123, as described in Table 3.19.

Table 3.18: A table indicating the results obtained between post cleaning of a wound with saline and risk for antibiotic resistance.

<table>
<thead>
<tr>
<th>Total number of organisms post-clean</th>
<th>Low risk</th>
<th>High risk</th>
<th>Total number of individuals according to number of organisms post-clean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly mixed</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>1 microbe count</td>
<td>18</td>
<td>18</td>
<td>36</td>
</tr>
<tr>
<td>2 microbes count</td>
<td>15</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td>3 microbes count</td>
<td>2</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Total number of individuals according to risk</td>
<td>38</td>
<td>42</td>
<td>80</td>
</tr>
</tbody>
</table>

\( \chi^2 = 8.580, p \text{- value} = 0.035 \)
Table 3.19: A table indicating the significance of microbes identified post-cleaning of the wound with the severity of wound infection and risk for antibiotic resistance.

<table>
<thead>
<tr>
<th>Severity/ Risk</th>
<th>Highly mixed</th>
<th>1 microbe</th>
<th>2 microbes</th>
<th>3 microbes</th>
<th>Total number of individuals according to Severity/Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR/S</td>
<td>0</td>
<td>11</td>
<td>10</td>
<td>10</td>
<td>31</td>
</tr>
<tr>
<td>LR/S</td>
<td>2</td>
<td>13</td>
<td>11</td>
<td>2</td>
<td>28</td>
</tr>
<tr>
<td>NS/LR</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>HR/NS</td>
<td>1</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>11</td>
</tr>
</tbody>
</table>

Total number of individuals according to number of organisms post-clean

χ²: 13.969 p-value: 0.123
### 3.6 Post-Clean of Wound Twice with Saline Culture

#### RESULTS

Table 3.20 and Figure 3.7 describe the cultures which were identified in the post clean wound swabs. Table 3.20 describes all the cultures obtained and their frequency when observed, whilst the pie chart in Figure 3.7 describes the percentage of microbes obtained, in groups: MRSA spp, MSSA spp., *Proteus and Morganella* spp, *Enterococci* spp, *E. Coli* spp, *Streptococci* spp., *Pseudomonas* spp., Others spp.

Table 3.20: A table indicating all the species present in the post- clean wound swab.

<table>
<thead>
<tr>
<th>Name of organism</th>
<th>Quantity observed in Wound Swabs post clean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly Mixed</td>
<td>4</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>22</td>
</tr>
<tr>
<td>MRSA</td>
<td>17</td>
</tr>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td>5</td>
</tr>
<tr>
<td><em>Acinetobacter lwoffi</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>14</td>
</tr>
<tr>
<td><em>E.coli</em></td>
<td>10</td>
</tr>
<tr>
<td>Group G Haemolytic Strept</td>
<td>1</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>28</td>
</tr>
<tr>
<td><em>Citrobacter koseri</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>16</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Morganelli morganii</em></td>
<td>6</td>
</tr>
<tr>
<td><em>Achromabacter dentrificans</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Staphylococcus epididermis</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Clostridium perfingens</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Myroides</em> spp</td>
<td>1</td>
</tr>
<tr>
<td><em>Proteus vulgaris ESBL+VE</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Citrobacter brakii</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>0</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Klebsiella pneumonia</em></td>
<td>2</td>
</tr>
</tbody>
</table>
Figure 3.4: A pie chart indicating the percentage of groups of microorganisms identified in the post-cleaning of the wound twice with saline as advised by the MDH Antibiotic team.
3.7 CONCORDANCE OF WOUND SWABS CULTURE AND SENSITIVITY RESULTS WITH ANTIBIOTICS ADMINISTERED

Table 3.21 indicates that the mean wound improvement was not affected by wound sensitivity results. However, mean values obtained indicate that those 34 individuals who obtained concordant results with the wound swab sensitivity tests, proved to have obtained higher mean values, indicating that the non-significance obtained could have been a result of the small population sample size present. When concordance was evaluated through a chi-squared test; using severity parameters, no statistical significance was observed. A p-value of 0.063 was obtained. However when severity and risk were assessed, the p-value obtained was of 0.001, hence indicating that severity/ risk factor and concordance are related, as described in Table 3.22.
Table 3.21: A table indicating the wound improvement with compliance to wound swab sensitivity result. (Were yes: concordant with wound swab results, no: not concordant with wound swab results, partial: that there was partial concordance with wound swab results, and not available: that no sensitivity results were achieved, as culture result obtained was highly mixed, hence no sensitivities were present).

<table>
<thead>
<tr>
<th></th>
<th>Number of Participants</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Standard Error</th>
<th>95% Confidence Interval for Mean</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
</tr>
<tr>
<td>Yes</td>
<td>34</td>
<td>17.15</td>
<td>8.753</td>
<td>1.501</td>
<td>14.09</td>
<td>20.20</td>
</tr>
<tr>
<td>No</td>
<td>23</td>
<td>16.57</td>
<td>9.395</td>
<td>1.959</td>
<td>12.50</td>
<td>20.63</td>
</tr>
<tr>
<td>Partial</td>
<td>19</td>
<td>15.95</td>
<td>5.835</td>
<td>1.339</td>
<td>13.13</td>
<td>18.76</td>
</tr>
<tr>
<td>Not available</td>
<td>4</td>
<td>13.25</td>
<td>4.924</td>
<td>2.462</td>
<td>5.41</td>
<td>21.09</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>16.50</td>
<td>8.127</td>
<td>0.909</td>
<td>14.69</td>
<td>18.31</td>
</tr>
</tbody>
</table>
Table 3.22: A table indicating the number of individuals who were concordant with the wound swab sensitivity results in view of severity and risk parameters and the \( p \)-value obtained. Where Hr: high risk, S: severe, LR: low risk, NS: non-sever.

<table>
<thead>
<tr>
<th>Severity/Risk</th>
<th>Concordance</th>
<th>Total number of individuals according to severity/risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>HR/S</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>LR/S</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>NS/LR</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>HR/NS</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total number of individuals according to concordance</strong></td>
<td>34</td>
<td>23</td>
</tr>
</tbody>
</table>

\( \chi^2: 26.923 \) \( p \)-value:0.001

The general linear model in Table 3.23, describes that concordance with wound swab result was not a strong determinant of wound healing, but when \( p \)-values are compared, those results which were found to be concordant obtained \( p \)-values nearer to the 0.05 level of significance. Additionally, mean values also highlight that when concordance results were compared with individuals who concordance was not available, a mean difference is noted. The quantity of microbes present in a wound, was also indicative of improvement in the wound, where the larger the number of microbes the less the improvement in the wound, although this value was not strong enough to provide a significant difference.
Table 3.23: A table indicating a general linear model for compliance with algorithm, concordance with wound swab posts clean and number of organisms in post-clean wound swabs.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Standard Error</th>
<th>T</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>10.638</td>
<td>4.120</td>
<td>2.582</td>
<td>0.012</td>
</tr>
<tr>
<td>Compliance: Yes</td>
<td>5.224</td>
<td>2.018</td>
<td>2.588</td>
<td>0.012</td>
</tr>
<tr>
<td>Compliance: No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Concordance: Yes</td>
<td>4.506</td>
<td>4.728</td>
<td>0.953</td>
<td>0.344</td>
</tr>
<tr>
<td>Concordance: No</td>
<td>3.738</td>
<td>4.860</td>
<td>0.769</td>
<td>0.444</td>
</tr>
<tr>
<td>Concordance: Partial</td>
<td>3.075</td>
<td>4.771</td>
<td>0.644</td>
<td>0.521</td>
</tr>
<tr>
<td>Concordance: Not Available</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Highly mixed post clean</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1 microbe post clean</td>
<td>1.979</td>
<td>2.789</td>
<td>0.710</td>
<td>0.480</td>
</tr>
<tr>
<td>2 microbes post clean</td>
<td>0.112</td>
<td>2.892</td>
<td>0.039</td>
<td>0.969</td>
</tr>
<tr>
<td>3 microbes post clean</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
3.8 OTHER FACTORS WHICH COULD AFFECT WOUND IMPROVEMENT

Other factors were also assessed in order to determine whether wound improvement was influenced by other factors. Results were as described in Table 3.24.1 and 3.24.2. Although most of the parameters describe a non-statistically significant \( p\)-value, mean results do describe that there were differences in the results. A reason why statistical significance was not observed in these parameters could have resulted from the small population size.

Table 3.24.1: Table indicating the mean values and \( p\)-values for other factors which might have influenced the wound improvement (Part one).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>( p)-value</th>
<th>Significance</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.832</td>
<td>Not Significant</td>
<td>Female: 16.76; Male: 16.35</td>
</tr>
<tr>
<td>Age Group</td>
<td>0.963</td>
<td>Not Significant</td>
<td>&lt;60 years: 16.44; 61-70 years: 16.10; 71-80 years: 17.20; &gt;80 years: 16.05</td>
</tr>
<tr>
<td>ABPI</td>
<td>0.460</td>
<td>Not Significant</td>
<td>&lt;0.5: 16.30; 0.5-0.8: 17.11; 0.8-1: 15.30; 1-1.3: 11.80; Calcification: 18.93</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>0.481</td>
<td>Not Significant</td>
<td>Yes: 17.00; No: 15.67</td>
</tr>
<tr>
<td>Venous Ulcer</td>
<td>0.073</td>
<td>Not Significant</td>
<td>Yes: 12.20; No: 17.11</td>
</tr>
<tr>
<td>Arterial Ulcer</td>
<td>0.312</td>
<td>Not Significant</td>
<td>Yes: 17.43; No: 15.58</td>
</tr>
<tr>
<td>Mixed Ulcer</td>
<td>0.617</td>
<td>Not Significant</td>
<td>Yes: 14.50; No: 16.61</td>
</tr>
<tr>
<td>Neuroischaemic</td>
<td>0.529</td>
<td>Not Significant</td>
<td>Yes: 17.50; No: 16.17</td>
</tr>
<tr>
<td>Neuropathic Ulcer</td>
<td>0.756</td>
<td>Not Significant</td>
<td>Yes: 15.50; No: 16.58</td>
</tr>
<tr>
<td>Pressure Ulcer</td>
<td>0.914</td>
<td>Not Significant</td>
<td>Yes: 17.00; No: 16.48</td>
</tr>
</tbody>
</table>
Table 3.24.2: Table indicating the mean values and $p$-values for other factors which might have influenced the wound improvement (Part 2).

<table>
<thead>
<tr>
<th>Factor</th>
<th>$p$-value</th>
<th>Significance</th>
<th>Yes:</th>
<th>No:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDDM</td>
<td>0.061</td>
<td>Not Significant</td>
<td>18.29</td>
<td>14.88</td>
</tr>
<tr>
<td>NIDDM</td>
<td>0.462</td>
<td>Not Significant</td>
<td>15.70</td>
<td>17.06</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0.249</td>
<td>Not Significant</td>
<td>16.98</td>
<td>14.21</td>
</tr>
<tr>
<td>Aspirin</td>
<td>0.737</td>
<td>Not Significant</td>
<td>16.62</td>
<td>15.73</td>
</tr>
<tr>
<td>Diuretic</td>
<td>0.388</td>
<td>Not Significant</td>
<td>16.86</td>
<td>14.79</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.289</td>
<td>Not Significant</td>
<td>16.85</td>
<td>13.78</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>0.299</td>
<td>Not Significant</td>
<td>13.17</td>
<td>16.77</td>
</tr>
<tr>
<td>Renal Patient</td>
<td>0.095</td>
<td>Not Significant</td>
<td>11.17</td>
<td>16.93</td>
</tr>
<tr>
<td>Hepatitis B +ve</td>
<td>0.854</td>
<td>Not Significant</td>
<td>18.00</td>
<td>16.48</td>
</tr>
<tr>
<td>Smoker</td>
<td>0.468</td>
<td>Not Significant</td>
<td>14.92</td>
<td>16.78</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.978</td>
<td>Not Significant</td>
<td>16.60</td>
<td>16.49</td>
</tr>
<tr>
<td>Pain Killers</td>
<td>0.007</td>
<td>Significant</td>
<td>18.85</td>
<td>14.03</td>
</tr>
<tr>
<td>Steroids</td>
<td>0.115</td>
<td>Not Significant</td>
<td>22.75</td>
<td>16.17</td>
</tr>
<tr>
<td>Anti-depressants</td>
<td>0.425</td>
<td>Not Significant</td>
<td>14.14</td>
<td>16.73</td>
</tr>
<tr>
<td>Thyroxin</td>
<td>0.541</td>
<td>Not Significant</td>
<td>20.00</td>
<td>16.41</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>0.950</td>
<td>Not Significant</td>
<td>16.25</td>
<td>16.51</td>
</tr>
<tr>
<td>Aortic Valve Replacement</td>
<td>0.759</td>
<td>Not Significant</td>
<td>19.00</td>
<td>16.47</td>
</tr>
<tr>
<td>Congestive heart Failure</td>
<td>0.294</td>
<td>Not Significant</td>
<td>13.63</td>
<td>16.82</td>
</tr>
<tr>
<td>Alginate</td>
<td>0.029</td>
<td>Significant</td>
<td>13.39</td>
<td>17.75</td>
</tr>
<tr>
<td>Inadine</td>
<td>0.251</td>
<td>Not Significant</td>
<td>17.06</td>
<td>14.56</td>
</tr>
<tr>
<td>Silver</td>
<td>0.408</td>
<td>Not Significant</td>
<td>14.86</td>
<td>16.85</td>
</tr>
<tr>
<td>Negative Pressure</td>
<td>0.662</td>
<td>Not Significant</td>
<td>19.00</td>
<td>16.44</td>
</tr>
<tr>
<td>Four Layer Bandage</td>
<td>0.071</td>
<td>Not Significant</td>
<td>11.89</td>
<td>17.08</td>
</tr>
</tbody>
</table>
The general linear model in Table 3.25, indicates that although no significant $p$-value was obtained, when analysing the improvement of the wounds with revascularization, and four layer bandage, the mean wound improvement results indicate that there was a difference in the mean wound improvement when revascularization and four layer bandage were used. Although not the same $p$-value was obtained, the results of the general linear model (GLM) are coherent with the results obtained for the ANOVA testing. Although the p-values are not the same, the GLM provides more accurate results, as the parameters are assessed on their own.

Table 3.25: A table indicating the general linear model for revascularization procedure and four layer bandage as treatment modalities.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean wound improvement</th>
<th>Standard Error</th>
<th>t</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intercept</strong></td>
<td>17.043</td>
<td>1.685</td>
<td>10.113</td>
<td>0.000</td>
</tr>
<tr>
<td><strong>Revascularization: Yes</strong></td>
<td>0.060</td>
<td>2.011</td>
<td>0.030</td>
<td>0.967</td>
</tr>
<tr>
<td><strong>Revascularization: No</strong></td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Four Layer Bandage: Yes</strong></td>
<td>5.161</td>
<td>3.080</td>
<td>1.675</td>
<td>0.098</td>
</tr>
<tr>
<td><strong>Four Layer Bandage: No</strong></td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Although ANOVA testing in Table 3.24.1 resulted in no statistically significant difference between wound improvement in individuals who had insulin dependent diabetes mellitus (IDDM) and those with non- insulin dependent diabetes mellitus (NIDDM). The
general linear model in Table 3.26, which assesses the parameters on their own, identifies a statistically significant difference when the two factors are compared. Results indicate that individuals who suffered with IDDM achieved better results than those who suffered from NIDDM.

Table 3.26: A table indicating the general linear model for IDDM (Insulin dependent Diabetes Mellitus) and NIDDM (Non-Insulin dependent Diabetes Mellitus).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean wound improvement</th>
<th>Standard Error</th>
<th>t</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>11.889</td>
<td>2.655</td>
<td>4.479</td>
<td>0.000</td>
</tr>
<tr>
<td>IDDM: Yes</td>
<td>6.401</td>
<td>2.952</td>
<td>2.168</td>
<td>0.033</td>
</tr>
<tr>
<td>IDDM: No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NIDDM: Yes</td>
<td>3.808</td>
<td>2.995</td>
<td>1.272</td>
<td>0.207</td>
</tr>
<tr>
<td>NIDDM: No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

The results which were obtained in this study will be discussed in the following Chapter together with a discussion on the possible reasons as to why these results were obtained, and how the data obtained compares with similar studies.
CHAPTER 4
DISCUSSION
4.1 INTRODUCTION

Overall the results obtained indicate that the algorithm derived by Mater Dei Hospital (MDH) Antibiotic Team was validated through the methodology used in this study. Thus prescribers can be more confident and encouraged when using the MDH algorithm. Furthermore this study highlighted the need for proper wound cleaning prior to taking a wound swab for culture and sensitivity.

4.2 VALIDATION OF THE LOWER LIMB WOUND AND ULCER ALGORITHM BY MATER DEI ANTIBIOTIC TEAM

The results obtained in this study determine that all individuals showed improvement in wound healing, except for one. Out of the 80 participants taking part in this study, 47 participants were compliant with the algorithm and all of them showed improvement in all the wound parameters. Tables 3.6 and 3.21 (pgs. 74, 90 respectively), show that the average improvement was highest in individuals who were high risk to antibiotic resistance and had results from wound swabs which provided concordant sensitivity results with the antibiotics administered. On the other hand, improvement, was lowest in those patients who were low risk to antibiotic resistance and concordance with sensitivities from wound swab results was indeterminate since post clean wound swab result were highly mixed, and no organisms could be identified. It is to be pointed out however, that the results obtained could have been different should the number of patients have been larger.
As described in Tables 3.4 and 3.5 (pgs. 72, 73 respectively), the algorithm for lower limb wounds and ulcers derived by the MDH antibiotic team was validated by this study since, the mean wound improvement observed in the patients who were compliant with the MDH algorithm, had a higher rate of improvement in the wound. The results for validation are further supported, when the one-way ANOVA testing was performed. This test indicates that there was a statistically significant difference between compliant and non-compliant participants with the algorithm, with a \( p \)-value of 0.010. These results indicate that in those individuals who had been treated as recommended by the MDH algorithm, obtained a noticeably higher mean in wound improvement than those who were not treated as recommended by the MDH algorithm (13.73: 18.45).

The general linear model described in Table 3.16 (pg 81), also determines that there was a statistically significant difference in the results between the individuals who were given antibiotics compliant to the algorithm, and those who were not. This result is supported by the results of the ANOVA testing described above. Hence it can be concluded that the MDH algorithm for the treatment of lower limb wounds or ulcers is validated. Furthermore the results indicate the importance of adherence to the algorithm since improvement in wounds or lower limb infections is increased with compliance.

Moreover, although multiple factors were assessed using multiple regression models, compliance with the MDH algorithm was one of the two factors which provided a statistically significant difference when wound improvement was assessed. This result further highlights the importance of adherence with the wound algorithm provided by MDH antibiotic team.
As described earlier, in section 1.1, no other studies validating algorithms or guidelines are available in the published literature; hence no comparison with other similar studies could be made. This accentuates the novel aspect of this study.

Risk for antibiotic resistance was one factor where, statistical tests provided a non-statistically significant \( p \)-value for wound improvement; even though mean values indicate that high risk participants obtained better results. Hence indicating that mean wound improvement was higher in individuals who were at high risk to antibiotic resistance than those who were at a low risk to antibiotic resistance. This result was unanticipated since high risk individuals might have been administered antibiotics previously, which could result in development of resistance organisms (Ambrosh et al., 2011) thus decreased improvement in wound. This result could be attributed to the reasoning that although high risk individuals might have had worse condition wounds, these might have achieved a greater range of improvement than those wounds that were low risk. As described in various articles (French, 2010, Piddock, 2012, Bush et al, 2011, Spellberg et al, 2007), the escalation of antibiotic resistance worldwide is highlighting urgent need to use antibiotics properly. The results from this specific study identify the need to use with responsibility antibiotics in order to decrease the risks of the development of antibiotic resistance, even though results indicate that high risk participants obtained a greater wound improvement than low risk participants.

Ulcer wound severity was also statistically assessed. Results in Table 3.7 (pg. 74), show that those who presented with a severe infection obtained better results than those who presented with a non-severe infection. This could have resulted from the fact that the antibiotics indicated were more appropriate to the microorganisms present in the severe patient groups. Moreover non-severe infections require less effort to obtain improvement. It
could also have resulted from the fact that non-severe infection patients did not, in fact have an infection. As described in the literature review, it is difficult to identify between colonization and wound infection, and its diagnosis and management is detrimental and also corroborated by the physician attending to the patient (Edwards, Harding, 2004).

4.3 Efficacy of Wound Cleansing Prior to Taking a Wound Swab

As described in Figure 3.3, and Tables 3.17 (pgs. 82, 84 respectively), a difference was noted between the pre-cleaning of wound swab group and the post-cleaning of wound swab group. In fact, the results obtained showed that there was a decrease in number of microorganisms in a wound in 67.5% of the cases assessed. In fact, the number of individuals who had a mixed culture decreased from 47.5% in the pre-cleaning of the wound swab results, to 5% in the post-cleaning wound swab results.

The results stress the importance of proper wound cleaning prior to taking a wound swab in order to identify as much as possible the infecting organisms. The method recommended by the MDH algorithm provided a statistically significant result with a $p$-value lower than 0.01, when the number of organisms obtained pre-cleaning and post cleaning was determined.

Although various articles provide information with regards to the decreased reliability of wound swab from deep tissue cultures, no data, as yet has been identified comparing multiple techniques of wound swabbing. Hence, it is also important to keep in mind the
method used to take a wound swab in other studies, since this might have influenced the results. Metluoglu et al, 2011, described that in individuals with diabetic foot wounds, the wound swab was an unreliable method for guidance of antimicrobial therapy, when compared with deep tissue wound swabs. Moreover, the accuracy of the superficial wound swabs compared to deep tissue culture was 73%. Metluoglu et al, 2011, however describe, that there was no specification of how many times the wound was cleansed prior to taking the wound swab. The author suggests that should these results have been used for antibiotic prescription, 32.5% of participants would have been mistreated.

Consistent with these results was a study presented by Lim et al, 2006, which described that biopsy procedures provide better results for microbiological profiling. Other authors, Bozkurt et al, 2011, Slater et al, 2003, do not agree with this conclusion, and they state that although other methods of identifying wound infection might be more effective, swab cultures provide valuable information should there be no bone involvement (Lim et al, 2006, Slater et al, 2003, Bozkurt et al, 2011). Nonetheless, the methodology for taking a wound swab was very unclear in most of the studies mentioned, and hence results could have been different due to this fact.

A numbers of organisms in post-clean wound swabs were found to be only affected by risk. However, when severity or severity/ risk were assessed, no statistically significant difference was noted. This indicates, that as described earlier, by Eleftheriadou et al, 2010, the risk for antibiotic resistance, which includes; previous antibiotic administration, residency in a hospital etc., does result in an increased number of organisms present in a wound.
Furthermore the results obtained stress, the importance of taking a proper wound swab. In a small scale study on nurses' practices in the UK in 2003, a need for guidelines which would help the nurse on how to properly acquire a good wound swab was highlighted, as the practice used was found to be extremely different between different categories of nurses. This need was identified, as inappropriate use of wound swabs results in inappropriate treatment modalities, patient morbidity and a drastic increase in hospital stays (Starr, MacLeod, 2003). In fact, various NHS trusts in the UK have designed their own guidelines for the proper procedure of taking a wound swab (Procedure for taking a wound swab, 2008). This highlights that the validity and reliability of the results from a wound swab is affected by the proper technique.

Moreover the data obtained provides information supporting the importance of proper wound cleaning, this indicates the need for further studies which can identify the best protocol for wound cleansing prior to taking a wound swab. This means that further studies can be conducted to identify different methods of cleaning. Results obtained will then in turn provide guidelines on the proper cleansing method of the wound before taking a wound swab.

4.4 WOUND MICRO FLORA OBSERVED IN THE STUDY

Our study identified that the most common organisms observed in the wounds post-cleaning were as those described in Figure 3.4

As described in a study by Diamantopolus et al, 1998, the majority of diabetic foot wounds present with multiple microbes. In fact, in our study, 36 individuals (45%), presented with one organism, while 55% (44 individuals) presented with more than one organism.
Diamantopoulos et al, 1998, identified that the majority of microbes as aerobic (3:1 versus anaerobe organisms).

In our study, however, it was found that the majority of the organisms which were most likely to be causing infection where mainly facultative anaerobes, which are able to adapt to growing in both oxygen deprived and oxygen rich environments, even though they do prefer aerobic environments (Stieglmeier et al, 2009). This was followed by anaerobes and aerobes, 33%: 21%: 13% respectively. Hence the results obtained in our study which describe the most probable offending organisms do not reflect what has been noted by Diamantopoulos et al, 1998.

Calhoun et al, 2002 described that the most common microbe which is present in diabetic wound infections is Staphylococcus aureus, facultative streptococci spp are noted in about one third of the populations studied, whilst anaerobes are uncommon. Our results as described in Figure 3.4 (pg. 88) indicate that the MSSA and MRSA were the most common microbes identified, followed by enterococci species, hence indicating that our results correspond to the total number of organisms reported in the review by Calhoun et al, 2002.

Our results do not concur with what was obtained by Alsaimary, 2008 where the author identified that the most common micro-organism present was Staphylococcus saprophyticus, and Staphylococcus aureus was present in only 4% of the population. This difference in the results could be attributed to the difference in the world region from where the population was chosen from, (Basrah in Iran) (Alsaimary, 2008). Eleftheriadou et al, 2010, described an increase in the number of MRSA in patients who were hospitalised. In this study, MRSA, even though it was not the main probable infecting organism, was present in
wounds identified for this study. The amount is very similar to what has been found by this author, who found that 15-30% of the wounds presented with MRSA. This value is very similar to the 14% MRSA present in post-cleaning wound swab results obtained in our study.

4.5 CONCORDANCE OF ANTIBIOTICS WITH WOUND IMPROVEMENT

The majority of the individuals who participated in this present study had full concordance between the antibiotics administered and the wound swab sensitivity result post-wound cleaning as described in Table 3.21 (pg. 90). Dr Bjarnsholst et al, 2008 described that individuals who were given inappropriate antibiotics for acute wounds, might develop into a chronic wound. Hence, it is of utmost importance to use appropriate antimicrobial therapy. Our study identified that the concordance of antibiotics with the wound swab and wound improvement does not provide a statistically significant result. However, the mean wound improvement in wounds which were concordant with the wound swab result did show a greater improvement (17.15). The general linear model described in Table 3.23, (pg. 92) also shows this concordance. Although p-value is not statistically significantly different, the mean results indicate that individuals who were concordant with post-clean wound culture and sensitivity results, obtained an increased mean improvement in wound by a factor of 4.506 more than those who did not have an available result for concordance due obtaining a mixed culture.

This discrepancy could again have resulted from the small sample size in our study which when the patients were further divided as concordant, not concordant, partial concordance and no available concordance with wound swab sensitivity result, further
decreased the sample size. Concordance also does not relate with risk and severity. However, when severity and risk where assessed simultaneously, a significant \( p \)-value was obtained, hence indicating that together they did affect the concordance of antibiotics with the wound swab.

Thus these results indicate that concordance with wound swab result is important although no statistically significant result was obtained. Furthermore, as described by Hobizal and Wukich, 2012, optimal antibiotic therapy should be based on results obtained from culture and sensitivity testing (Hobizal, Wukich, 2012). Other factors to be taken into consideration when prescribers advise antibiotic therapy include cost, side effects of the drug, pharmacokinetics, bioavailability, frequency and route of the drug (Hobizal, Wukich, 2012). These should be taken into account in order to improve adherence to therapy by the patients, with the lowest cost and the best pharmacological effectiveness for the patient.

### 4.6 Other Factors Which Might Affect Wound Healing

There are various parameters which could affect the rate of improvement of a wound. These were assessed in this present study, but most of them proved to be non-significant except for pain killers and alginate dressing. Only these parameters significantly affected the rate of wound healing.

Other factors were assessed, and were identified to have resulted in a difference in the wound improvement. Although they might not have been statistically significant; however they showed a difference indicative of an effect on the wound improvement as described below.
4.6.1 STEROIDS

A study conducted by Alberti et al, 2012, described that the use of local and systemic steroids, result in reduced wound healing in the first week post-operatively. This could be due to the delayed deposition of collagen fibres, hence resulting in hindered skin wound healing. However, other studies are required in order to identify the proper pathophysiology justifying why steroids affect wound healing (Alberti, de Souza Vasconcellos, Petroianu, 2012).

Wang et al, 2013, on the other hand, conducted a systematic review which concluded that acute high doses of corticosteroids do not effect wound healing, whilst chronic use of systemic steroids was shown to impair wound healing (Wang, Armstrong, Armstrong, 2013). These results as already discussed do not coincide with what was observed in our study, since no statistically significant difference was observed as shown in Table 3.24.1 (pg. 93), where a difference in the mean value for wound improvement has been observed. A study by Bergkvist and Sjobeck, 1998, describes that corticosteroids can be administered and will help in improving the rate of wound healing in individuals with "no exclusion criteria". This includes conditions such as diabetes. This has also been cited in the guidelines by the Infectious Disease Society of America (IDSA), where they recommend the use of corticosteroids for cellulitis cases, but not in diabetic individuals. (Stevens et al, 2014)

However, the steroids administered in this study were not in concordance with antimicrobial therapy, and no indication has been given in this study as to whether the steroids were given in acute or chronic doses. This is a limitation for this test result and, hence further studies need to be performed in order to further assess the effect of steroids on wounds.
4.6.2 ANTIPLATELET AND ANALGESICS

Most of the patients participating in this study were being given analgesics. This proved to affect the rate of wound healing. In fact it resulted in a statistically significant effect on the rate of wound healing. A study by McGuire et al, 2006, concluded that pain did affect the rate of wound healing. In fact the higher the pain intensity recorded by the patient, the slower the healing process (Mc Guire et al, 2006). In a review by Stein and Kuchler, 2013, it was discussed that topically applied opioids might enhance wound healing. Although no clinical trials have been undertaken, it is regarded that, cell migration and wound closure are more likely with the use of morphine (Stein, Kuchler, 2013). These results coincide with what has been found in this study as observed in Table 3.24.2, (pg. 94) and indicate that analgesics do have a positive effect on the rate of wound healing.

Aspirin which has both analgesic and antiplatelet effect was being used by 69 individuals (86.25%) in our study. Wound healing was found not to be significantly affected by aspirin, although a mean difference was found to be noted as observed in Table 3.24.2, (pg. 94), where individuals who had been taking aspirin obtained a better result in wound improvement than those who did not take aspirin.

As described in a study by Santos and Monte- Alto- Costa, 2013, wound healing was found to be delayed only in the female gender in a pre- clinical study on mice, whereas the male gender was not affected (Dos Santos, Monte- Alto- Costa, 2013). This was confirmed in this study, 86.25% of the participants had been taking aspirin, and out of these, 63.8% were males, indicating that the results obtained in mice do reflect what is observed in humans. Although further studies need to be done in order to further confirm and strengthen these
results since, the mean differences did show a small degree of difference with aspirin in the mean improvement.

4.6.3 OXYGENATION AND REVASCULARIZATION

In a review by Gotrup, 2004, the importance of proper oxygenation of the wound, which is described as microvasculature to the wound, is discussed. Lack of oxygenation increases the risk of infection; hence it is important to have an adequate blood supply to the wound for appropriate oxygenation and nutrients in the wound area (Tandara, Mustoe, 2004). As described in Figure 1.5 (pg. 37), there are multiple factors which contribute to the hypoxia of the wound area and these also result in other complications such as infections and inflammation. Our results did not provide a statistically significant result when ABPI and revascularization were assessed, even though linear models suggest an increase in wound improvement of a factor of 0.06 in individuals who had revascularization, than those who did not.

This does not mean that these factors are not significant, but as described earlier, a limitation of this present study was the number of participants recruited in this study which might have resulted in a decreased significance of the importance of revascularization and ABPI. Zammit et al, 2011, described that lower doses of gentamicin are noted in individuals with severe peripheral arterial disease. This indicates that peripheral arterial disease hinders the rate of blood flow to the wound, hence decreasing the oxygen and nutrient supply to the wound impeding healing (Zammit et al, 2011, Schreml et al, 2010).
Furthermore, in a study conducted by Formosa et al, 2012, the importance of assessing the vascular supply, was highlighted since, a proportion of the Maltese population who are diabetic, have noticeable vascular insufficiency. This indicates that vascular supply is not adequate to the lower limbs, and thus increases the risks for non-healing wound ulcers (Formosa et al, 2012). However our results describe a difference in the mean values obtained in the revascularization and in the ABPI parameters. These results found that the individuals who have had a revascularization procedure obtained a greater mean wound improvement result than those who did not have a revascularization procedure. Hence indicating that although the sample size was not large enough to indicate a statistically significant difference, a difference was noted and this highlights the need for further studies on this issue.

4.7 **INSULIN DEPENDENT DIABETES MELLITUS AND NON INSULIN DEPENDENT DIABETES MELLITUS**

Diabetes is a condition which affects multiple organs in the body resulting in macro and micro complications, consequently risking loss of tissue viability which may result in wounds. In fact in our study, nearly 89% of the subjects were diabetic, with Insulin Dependent Diabetes Mellitus (IDDM) being more prevalent than Non-Insulin Dependent Diabetes Mellitus (Table 3.2, pg. 68).

In our study it was determined that wounds in participants, who were IDDM, did better than wound in individuals who were NIDDM. One possible explanation could be because of the smaller sample of participants suffering from NIDDM. This result could be due to better control of macro and micro complications which affects IDDM participants.
However, there is generally better glycemic control in IDDM participants through the use of insulin, when compared with NIDDM. As described by Gilliani et al., 2012, better glycemic control and better management of diabetes-related risk factors such as hypertension and hyperlipidema result in decreased macro and microvascular complications. Moreover Reiber, Boyoke, Smith, 1995 cite that in the Diabetes Control and Complications Trial, individuals who were IDDM had a better HbA1c value than the control group. This supports the results in our study, that IDDM participants obtained better results in wound improvement than NIDDM. Literature also describes that abnormally high glucose levels result in poor circulation, which will in turn result in ulcers which will be slow to heal, deep and become infected. Moreover uncontrolled diabetes will result in decreased ability of leukocyte function resulting in infections (Alsaimary, 2008).

4.8 LIMITATIONS OF THE STUDY

Firstly, the sample size selected, 80 patients is not a large enough sample. However, similar studies used between 40-60 patients, but 80 is limited especially since the population was further divided not just for compliance with the algorithm, but also for concordance with the wound. Moreover the population was also divided into individuals who had a revascularization procedure, and those who did not, and that further decreased the sample size. This small sample size was due to time and cost constrains. This sampling method is very prone to selection bias, and this could have been decreased by having a less heterogeneous population sample (LoBiondo-Wood, Haber, 2014).
Due to the nature of the study, no participants were recruited as controls. Should this have been done, results could have been further assessed and some underlying factors which were taken into consideration, such as medication, could have been further analysed in detail. Moreover it would have been interesting to study whether blood glucose level was also a determining factor. HbA1c would have given us a clear indication of the glucose control in either NIDDM or IDDM individuals and that would have given us an indication on whether appropriate glycemic control would have affected the rate of wound improvement. Moreover, no indication into the type of analgesia given was identified.

Furthermore, ankle brachial pressure index, (ABPI) was assessed, at the beginning of the study, prior to any revascularization procedures. Should a second reading for ABPI had been taken following revascularization, this would have aided to improve consistency in results, although the main aim of this study was to validate the wound algorithm.

Additionally, mobility was not assessed as a parameter; this could have resulted in differences in wound improvement between mobile and non-mobile individuals.

Another limitation of the study was that when both ABPI and BJWAT were taken, no one double checked that both the ABPI and the BJWAT were taken correctly. Although every effort was made to use correctly these tools, through expertise in the field, this might have resulted in a limitation.

Additionally, numbers were too small to identify any differences in the results which could have resulted from differences between different hospitals.
4.9 Recommendations for Future Studies

This study is novel, as this was the first of its kind to be conducted in the Maltese Islands. It was also the first to consider the validation of algorithms in the treatment of multiple organisms in foot ulcers.

Repeating this study with a larger number of participants and decreasing certain bias which might have affected certain results such as information on certain medications, could have yielded better results. Moreover, further information on parameters which affect the degree of lower limb wound improvement could be assessed, not only in the Maltese population but worldwide. Various parameters in this study could be assessed separately to determine possible causes of wound healing, resulting in more statistically significant results including other factors which might affect wound improvement in such population.

4.10 Recommendations for Practice

The stakeholders in lower limb wound care will benefit from this study when treated with antibiotics which are appropriate for their condition. Such studies are important as they will reduce the unnecessary use of inappropriate antibiotics. Hence, reducing hospital stays and costs for health care providers. Furthermore, appropriate wound swabbing techniques was found to provide more reliable information, which will in turn provide useful information for practitioners; with respect to antibiotic use and administration. Moreover, this will decrease the unnecessary costs for inappropriate wound swabs which may result in mixed culture results which in turn do not provide appropriate guidance for antibiotic administration.
Moreover, this study can be used in improving the algorithm by introducing pain control in order to provide the best quality of life for these patients throughout their hurdle with lower limb ulcers.

Moreover the results from this study will be presented to the MDH antibiotic team, and will be used to further support the use of this algorithm not just in MDH, but also in other hospitals in Malta. This data also provides an indication on the microbes which are more likely to infect a lower limb wound, hence guiding practitioners in foreseeing the probable wound infecting organisms.

4.11 CONCLUSION

In this study we can conclude that the recommendations for the treatment of lower limb wounds and ulcer guidelines developed in the MDH algorithm are valid. It is also important for the practitioners to adhere to these guidelines, since better wound improvement was noted in individuals who were compliant with the algorithm.

Furthermore it can be concluded that the importance of proper wound cleaning at least twice with saline prior to taking a wound swab. This will improve the reliability of the results obtained, and will properly guide antimicrobial choice. Moreover, it can be stated that although no statistically significant difference was identified when revascularization was assessed, those individuals who had a revascularization procedure were found to have had a better rate of wound improvement. Other parameters which might have also had an effect on the results obtained, although not statistically significant, need to be further analysed in order to conclude whether they are responsible for a change in wound improvement. Thus it is
recommended that the study is repeated with larger sample sizes, where further strengthening of indications obtained from our results would be tested further.
REFERENCES


References


51. Guideline algorithms for the antibiotic treatment of common infectious diseases in the hospital setting. Antibiotic team Mater Dei Hospital. 2012


APPENDIX 1
NHS Wirral
Antimicrobial Guidelines
for the Management of Common Infections in Primary Care

9th Edition
Approved by Wirral Drug and Therapeutics Committee - October 2012
Publication date - October 2012
Revision date - October 2013

Adopted for use by the Cheshire & Wirral Partnership NHS Foundation Trust
Adopted for use by the Wirral Community NHS Trust

All information is believed to be correct at the time of publication.
## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>3 - 5</td>
</tr>
<tr>
<td>Five Main Principles of Antibiotic Prescribing</td>
<td>6</td>
</tr>
<tr>
<td>Antibiotic Prescribing Strategies for Respiratory Tract Infections</td>
<td>7</td>
</tr>
<tr>
<td>1. Upper Respiratory Tract Infections</td>
<td>8 - 11</td>
</tr>
<tr>
<td>2. Lower Respiratory Tract Infections</td>
<td>11 - 13</td>
</tr>
<tr>
<td>3. Urinary Tract Infections</td>
<td>13 - 19</td>
</tr>
<tr>
<td>4. Skin and Soft Tissue Infections</td>
<td>19 - 23</td>
</tr>
<tr>
<td>5. Eyes</td>
<td>24</td>
</tr>
<tr>
<td>6. Sexual Health</td>
<td>25 - 28</td>
</tr>
<tr>
<td>7. Gastroenteritis</td>
<td>28 - 30</td>
</tr>
<tr>
<td>8. Central Nervous System Infections</td>
<td>31</td>
</tr>
<tr>
<td>9. Viral Infections</td>
<td>31</td>
</tr>
<tr>
<td>10. Parasite Infections</td>
<td>31</td>
</tr>
<tr>
<td>11. Antibiotic Prophylaxis</td>
<td>32 - 33</td>
</tr>
<tr>
<td>Paediatric Doses</td>
<td>34 - 35</td>
</tr>
<tr>
<td>References</td>
<td>36 - 37</td>
</tr>
<tr>
<td>Other Sources of Information</td>
<td>38</td>
</tr>
<tr>
<td>How to Obtain Antibiotic Resources</td>
<td>38</td>
</tr>
<tr>
<td>Appendix 1 - Antibiotic Monographs</td>
<td>39 - 43</td>
</tr>
<tr>
<td>Appendix 2 - Wirral Community NHS Trust Community Nursing Service</td>
<td>44 - 45</td>
</tr>
<tr>
<td>Appendix 3 - Sharing Good Practice</td>
<td>46</td>
</tr>
<tr>
<td>Appendix 4 - Members of the Working Group</td>
<td>47</td>
</tr>
</tbody>
</table>

## INTRODUCTION

**The Main Aims of the NHS Wirral Antimicrobial Guidelines**

- To provide a guide to the management of common infections in primary care.
- To encourage the rational and cost-effective use of antibiotics.
- To reduce the risk of patients developing disease caused by *Clostridium difficile* via rational use of antibiotics.
- To reduce the emergence of bacterial resistance.

This document is evidence-based where such evidence exists and has been produced in accordance with advice laid down in the Department of Health’s Standing Medical Advisory Committee Sub-Group on Antimicrobial Resistance. The guidelines take into consideration local sensitivity data and have been drawn up to provide ‘best guess’ therapy. These guidelines are not based on costs.

*Please be prepared to change therapy in the light of:*

- Culture results. (Please note that sensitivities for antimicrobials other than those recommended in the guidelines may be reported, but should only be prescribed where the guideline choices are inappropriate).
- Patient non-response or adverse reaction.
- Microbiological consultation.

The guidelines are not intended to be exhaustive. Doses quoted are for oral therapy in typical adults with normal renal and hepatic function. Be prepared to alter dosages in patients with impaired renal or hepatic function. Please refer to antibiotic monographs in Appendix 1 for further detail.

Where therapy has failed or special circumstances exist, advice can be obtained from Wirral Medical Microbiology, which operates a 24-hour, 365-day clinical microbiology service. Please feel free to phone the Microbiology Department by either contacting:

<table>
<thead>
<tr>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Clatterbridge Hospital switchboard 0151 334 4000 ext 4512 during normal working hours.</td>
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<tr>
<td>2) Arrowe Park switchboard 0151 678 5111 if out-of-hours.</td>
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</tbody>
</table>

Including as much clinical information as possible on the sample request form will allow the most appropriate sensitivities to be reported e.g. type of urine sample, antibiotics already tried, pregnancy, significant co-morbidities.

**Intravenous Antibiotics - Wirral Community NHS Trust Community Nursing Service**

(Also see Appendix 2 for more information)

The prescriber may wish to prescribe intravenous antibiotics if the intravenous route is required (e.g. suitable oral alternative not available or appropriate) and admission to hospital is either inappropriate or not possible (for clinical or domestic reasons).
Please discuss options with the Medical Microbiologist before prescribing intravenous antibiotics. If intravenous antibiotics are an appropriate choice please discuss options with the Wirral Community NHS Trust Community Nursing Service and endorse the Patient Medicines Administration Chart (PMAC) with “Discussed with the Microbiologist”.

Microbiology MUST be formally consulted before using Wirral Community NHS Trust Community Nursing Service for intravenous antibiotic administration. Patient Medicines Administration Charts (PMAC) that have not been endorsed with “Discussed with the Microbiologist” will be queried with the Prescriber.

**Long-Term Antibiotic Prophylaxis in Adults**

It is recognised that in certain clinical scenarios (end-stage COPD with repeated infected exacerbations, recurrent urinary tract infections associated with catheterisation, calculi or uroscopy) Secondary Care consultants may recommend long-term antibiotic prophylaxis, often using rotating agents. While this may confer short-term benefit to the patient, this must be balanced against the increased risk of long-term development of resistance. This is frequently seen in such patients and can result in therapeutic difficulties (such as requirement for in-patient therapy) when infection does arise.

In cases where long-term prophylaxis is used, it may be of benefit to have a review point to assess the continual need, balancing continued perceived benefit versus potential risks.

Long-term antibiotic prophylaxis can result in particular problems in patients known to be MRSA or multi-resistant coliform colonised and these patients should be discussed with the microbiologist.

The National Collaborating Centre for Chronic Conditions (2004) states that prophylactic antibiotics are not recommended for people with stable chronic obstructive pulmonary disease, due to concerns about antibiotic resistance and potential adverse effects.

**Penicillin Allergy**

All prescribers are reminded of the advice contained in the British National Formulary (BNF):

- Individuals with a history of anaphylaxis, urticaria, or rash immediately after penicillin administration are at risk of immediate hypersensitivity to a penicillin; these individuals should not receive a penicillin. Patients who are allergic to one penicillin will be allergic to all because hypersensitivity is associated with the basic penicillin structure. As patients with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics, they should not receive these antibiotics.
- Individuals with a history of a minor rash (i.e. non-confluent, non-pruritic rash restricted to a small area of the body) or a rash that occurs more than 72 hours after penicillin administration are probably not allergic to penicillin and in these individuals a penicillin should not be withheld unnecessarily for serious infections; the possibility of an allergic reaction should, however, be borne in mind. Other beta-lactam antibiotics (including cephalosporins) can be used in these patients.

**Current Statutorily Notifiable Diseases and Food Poisoning**

Doctors must inform the Consultant in Health Protection when attending a patient suspected of suffering from any of the diseases listed under Notifiable Diseases in Chapter 5 in the BNF. For the local contact, please telephone 0844 235 1255 (daytime 9am to 5pm).

For further details please go to the Health Protection Agency website - www.hpa.org.uk

**Things You Can Do to Make a Difference...**

- Do not prescribe antibiotics for simple coughs, colds and sore throats unless good reason as per NICE Guidance on Respiratory Tract Infections - Antibiotic Prescribing.
- Limit prescribing of antibiotics for uncomplicated cystitis to three days in otherwise healthy women (less than 60 years of age).
- Avoid prescribing antibiotics over the telephone, except in exceptional circumstances.
- Consider using a deferred antibiotic prescription.
- Use microbiology tests where appropriate before prescribing an antibiotic.
- Use antibiotic resources to assist in educating the public.

**Main Changes Since the Last Edition**

Each section has been reviewed to ensure that it is in line with the most up-to-date national and local guidance.

The main changes in this edition are:

- Additional guidance on when to treat AOM in children
- Risk factors for antibiotic resistant organisms in COPD
- Consideration of 3 day course of antibiotics for women > 60 years
- Prophylactic antibiotics for patients with indwelling catheter
- Facial cellulitis
- Recurrent vulvovaginal candidiasis

For guidance on potential pandemic influenza then please visit the Health Protection Agency website at www.hpa.org.uk.

The NHS Wirral Antimicrobial Guidelines can also be accessed electronically via the Wirral Medicines Management internet site at the following address:

http://mm.wirral.nhs.uk/document_uploads/formulary/AntimicrobialGuidelinesMagtofCommo
nlncfe201213.pdf

Please be aware that the electronic document will be the most up-to-date version of the NHS Wirral Antimicrobial Guidelines in between revision dates. There may be differences between the hard copy and electronic copy of the document.

At the end of this guide (Appendix 1) there is a section of antibiotic monographs to provide information about the recommended antimicrobials. These monographs are not intended to be exhaustive. If any further information is required, it is recommended that the BNF should be consulted.

- The traffic light system in the monograph section of the guidelines is used to highlight those antibiotics with the greatest propensity for causing C difficile infection.
- Any antibiotics coloured red or amber are more likely to cause C difficile infection whereas those coloured green are less likely.

Doses in this guideline are for adults with normal renal and hepatic function unless otherwise specified. Paediatric doses can be found on pages 34 to 35.

**Acknowledgements**

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FIVE MAIN PRINCIPLES

1. USE ANTIBIOTICS APPROPRIATELY
   Avoid antibiotics in viral and mild self-limiting infections.

2. USE NARROW SPECTRUM AGENTS
   Broad spectrum agents are generally more expensive and potentially more toxic than narrow spectrum agents. They also produce more super-infection problems because of their capacity to deplete the commensal ('normal') flora.
   For many indications first line therapy with amoxicillin is recommended in this guidance, rather than co-amoxiclav.

   Note: Use simple generic antibiotics first whenever possible. Avoid broad spectrum antibiotics (eg, co-amoxiclav, quinolones and cephalosporins) when narrow spectrum antibiotics remain effective as they increase risk of Clostridium difficile, MRSA and resistant UTIs. (Health Protection Agency).

3. USE WELL ESTABLISHED AGENTS
   Well established agents are preferable to novel ones because of the length of time required for the definition of adverse effects and interactions. Although the use of newer antibiotics such as quinolones is increasing, they should be reserved for serious infections in primary care. Overuse of these agents will lead to increasing resistance diminishing their vital role in the treatment of severe life threatening infections.

4. USE DIFFERENT AGENTS FOR DIFFERENT INDICATIONS
   Generally there is no such thing as a good or a bad agent but there is optimal therapy for particular types of patients, infections and infecting agents.

5. USE SHORT COURSES FOR UNCOMPLICATED INFECTIONS
   For example, uncomplicated cystitis in female adults less than 60 years of age can be treated with a 3 day course of antibiotics.

Antibiotic Prescribing Strategies for Respiratory Tract Infections (RTIs)
(Adapted from NICE Guidance on Respiratory Tract Infections - Antibiotic Prescribing)

Agree a no antibiotic or delayed antibiotic prescribing strategy for the following (see exceptions below where immediate prescribing strategy may be considered).
- Acute sore throat/acute pharyngitis/acute tonsillitis.
- Acute otitis media.
- Common cold.
- Acute rhinosinusitis.
- Acute cough/acute bronchitis.

Exceptions
Depending on clinical assessment of severity, an immediate prescribing strategy should be considered for:
- Children younger than 2 years with bilateral acute otitis media.
- Patients with otorrhoea who have acute otitis media.
- Patients with acute sore throat/acute pharyngitis/acute tonsillitis when 3 or more Centor criteria are present.

Offer immediate antibiotics or further investigation/management for patients who:
- Are systemically very unwell.
- Have symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital or intracranial complications).
- Are at high risk of serious complications because of pre-existing comorbidity. This includes patients with significant heart, lung, renal or neuromuscular disease, immunosuppression, cystic fibrosis, and young children who were born prematurely.
- Are older than 65 years with acute cough and 2 or more of the following, or older than 80 years with acute cough and 1 or more of the following:
  - Hospitalisation in previous year.
  - Type 1 or type 2 diabetes.
  - History of congestive heart failure.
  - Current use of oral glucocorticoids.

It is important to provide advice about the usual natural history of the illness and average total illness length.

For further information:
http://www.nice.org.uk/CG69
1 UPPER RESPIRATORY TRACT INFECTIONS

1. Acute Sore Throat

Most sore throats are viral and do not require an antibiotic. Throat swabs should not be carried out routinely. Consider a throat swab only in persistent infections, where there are systemic signs or family/institutional outbreaks. A delayed prescription strategy may be useful when it is felt safe not to prescribe an antibiotic immediately. Advise regular use of paracetamol or ibuprofen to relieve pain and fever.

Limit use of antibiotics as 90% resolve in 7 days without antibiotic therapy, and pain is only reduced by 16 hours.

Clinical prediction for the presence or absence of Group A beta-haemolytic streptococcus in acute sore throat in adults (GABHS):

**The Centor Criteria**
- Tonsillar exudate.
- Tender anterior cervical lymphadenopathy.
- Absence of cough.
- History of fever.
- If none of the above are present, less than 3% of patients will have GABHS.
- If 3 out of 4 of the above are present, then 40% of patients are likely to have GABHS.

First line:
- Phenoxymethylpenicillin (penicillin V) 500mg qds for 10 days
- Or Clarithromycin 250-500mg bd for 5 days (If allergic to penicillin)

Note:
- Ten days therapy with penicillin is required to eradicate carriage of GABHS. Prescribing of clarithromycin should be reserved for those patients with true penicillin allergy. BNF current duration recommendation is for 10 days, however this study shows 5 days is efficacious.

Information on the Management of AOM

If children have AOM and:
- Fever (>37.5°C) or vomiting
  Half of this group of patients would settle within 72 hours without antibiotics. 3 to 6 children would need to be treated with antibiotics in order for 1 extra child to benefit.
- There is no fever or vomiting
  For every 100 children with AOM without fever or vomiting 6 extra patients would suffer reduced pain at day 7 with antibiotics; 6 extra would suffer rash, diarrhoea or vomiting. So the number needed to treat equals the number needed to harm.

Delayed Prescriptions
- Use of delayed prescriptions plus a handout for parents for AOM in children who are not particularly ill reduced overall antibiotic prescribing for children by one fifth in one group practice.

First Line:
- Amoxicillin 500mg to 1g tds for 5 days
- Or Clarithromycin 250mg bd for 5 days (If allergic to penicillin)

Treatment failures:
- Co-amoxiclav 625mg tds for 5 days

1. Acute Ear Infections (AOM)

Recent studies have questioned the need for antibiotics in AOM. Antibiotics should not be routinely prescribed for uncomplicated AOM. Adequate analgesia may be all that is required. Swabs should always be taken from acute discharge.
Acute Sinusitis

Acute sinusitis nearly always follows an upper respiratory tract infection and is diagnosed by the presence of nasal blockage (obstruction/congestion) or nasal discharge (anterior/posterior nasal drip) with facial pain (or pressure) and/or reduction of, or loss of, the sense of smell, lasting for less than 12 weeks.

The following may be present:

- Nasal discharge - a thick, purulent, coloured discharge (especially green) is more likely to indicate bacterial involvement (unlikely with a clear discharge).
- Nasal blockage or congestion - usually bilateral and caused by rhinitis.
- Facial pain - may be described as pressure and localized over the infected sinus, or it may affect teeth, the upper jaw, or other areas (such as eye, side of face, forehead).
- In children, symptoms of rhinitis predominate with facial pain being less prevalent. There may also be ear discomfort (Eustachian tube blockage).

Antibiotics are not required for most people presenting with acute sinusitis. Analgesia may be all that is required. An intranasal decongestant (maximum 1 week) may help if nasal congestion problematics.

Consider a delayed antibiotic prescribing strategy.

**First line:**
Amoxicillin 500mg to 1g tds for 7 days

*or*
Doxycycline may be considered as an alternative (if allergic to penicillin):
Doxycycline 200mg on the first day followed by 100mg each day thereafter for a total of 7 days.
Swallow capsules whole with plenty of fluid at meal times. Avoid strong sunlight or sun lamps.
Not for use in children younger than 12 years.

**Treatment failures:**
Co-amoxiclav 625mg tds for 7 days

Chronic sinusitis is diagnosed by the presence of nasal blockage (obstruction/congestion) or nasal discharge (anterior/posterior nasal drip) with facial pain (or pressure) and/or reduction of, or loss of, the sense of smell, lasting for longer than 12 weeks. Compared with acute sinusitis, in chronic sinusitis:

- Loss of smell is more commonly described.
- Facial pain is less common.

Chronic sinusitis may last several months. Antibiotic therapy is not usually warranted and should only be used after further discussion or referral to a specialist.

**1d: Acute Otitis Externa**

Otomize® Ear Spray (dexamethasone 0.1%, neomycin 3250 units/ml)
Apply 1 metered spray to the affected ear(s) tds for a minimum of 7 days (continue for a further 7 days if symptoms persist)

*or*
Sofradex® ear drops (dexamethasone 0.05%, †ramycetin 0.5%, gramicicin 0.005%)
Apply 2 to 3 drops to the affected ear(s) tds for a minimum of 7 days (continue for a further 7 days if symptoms persist)

Analgesia should be recommended for pain relief. It is important that a combination product is used as topical steroids should not be used alone. Keep the ear dry. If there is no improvement after 2 weeks of topical treatment, refer to the open access aural dressing clinic for aural toilet (Clinic 2 Outpatient Department, Arrowe Park Hospital).

**2: Lower Respiratory Tract Infections**

The only indication for systemic antibiotics is perichondritis in which case a systemic anti-pseudomonal agent would be required.

Use Ciprofloxacin 500mg to 750mg bd for 7 days then review and consider ENT referral.

**Note:**
In confirmed pseudomonas infection topical acetic acid 2% (EarCalm®) may also be of value.

1e: Croup

Croup is usually a viral illness so antibiotics are not indicated. Only symptomatic treatment is required. Symptoms usually resolve within 48 hours, although occasionally they may last for up to a week.

**MRSA**

MRSA is typically resistant to many broad spectrum agents such as macrolide and quinolone antibiotics. Prescribing of inappropriate broad spectrum agents in patients colonised by MRSA disrupts the patient's normal flora and allows MRSA to increase in numbers. This renders the patient more vulnerable to (potentially severe) MRSA infection.

It is therefore of great importance to be aware of previous MRSA results prior to prescribing.

**Note:**
Low doses of penicillins are more likely to select out resistance. Do NOT use quinolone (ciprofloxacin, ofloxacin) first line due to poor pneumococcal activity. Reserve all quinolones (including levofloxacin) for proven resistant organisms.

2a: Bronchitis (Acute)

For people with acute bronchitis with no pre-existing conditions, antibiotics are not routinely recommended.

**Symptom resolution can take 3 weeks.**

Consider prescribing antibiotics for people who have a pre-existing condition that impairs their ability to deal with infection or is likely to deteriorate with acute bronchitis. This includes people:

- Who are over 75 years of age, with fever.
- With chronic obstructive pulmonary disease (COPD).
- With heart failure.
- Who are immunocompromised, including people with cancer or insulin dependent diabetes.

**Note:**
More than 90% of cases of acute bronchitis do not have a bacterial cause.

Purulent sputum can arise from either viral or bacterial infection. The presence of purulent sputum in isolation is not a predictor of bacterial infection.

If antibiotics are indicated, use empirical treatment:

**First line:**
Amoxicillin 500mg tds for 5 days

*or*
Doxycycline 200mg stat then 100mg od for 5 days in total
Assess the CRB-65 score for all people diagnosed with pneumonia:

Antibiotics are not normally required.

Exacerbations, antibiotics in last 3 months.

Give immediate care options include short-stay inpatient treatment or hospital-supervised outpatient treatment.

For people with a CRB-65 score of 2, arrange same-day assessment in secondary care. Secondary care options include short-stay inpatient treatment or hospital-supervised outpatient treatment.

For people with a CRB-65 score of 1, consider arranging same-day assessment in secondary care. For people with a CRB-65 score of 0, treatment at home is usually appropriate, depending on clinical judgement and available social support.

Give immediate IM benzylpenicillin or amoxicillin 1g PO if delayed admission life threatening.

Alternative Management:

Delayed antibiotic prescriptions have been shown to reduce antibiotic use. Using a combination of a patient information leaflet with a delayed prescription reduced antibiotic use more than using the delayed prescription alone. There is also evidence that delayed prescriptions decrease re-attendance rates for similar symptoms.

2b Asshins (Acute Exacerbation of)

Antibiotics are not normally required.

2c Bronchitis (Chronic - Acute exacerbation) / Acute exacerbation of COPD

Antibiotics are only required if exacerbation of COPD is associated with:

- A history of increased purulent sputum
- Without increased purulent sputum but has consolidation on chest radiograph or clinical signs of pneumonia

First line:

Amoxicillin 500mg tds for 5 days
Or

Doxycycline 200mg stat then 100mg od for 5 days in total

(If allergic to penicillin)

Treatment failures or resistance risk factors:

Co-amoxiclav 625mg tds for 5 days

Risk factors for antibiotic resistant organisms include co-morbid disease, severe COPD frequent exacerbations, antibiotics in last 3 months.

Levofloxacin 500mg od for 5 to 7 days would normally be reserved for patients with known carriage of proven resistant organisms.

Remember:

Patients with frequent exacerbations, who have received repeated courses of antibiotics, should have sputum samples submitted for each additional exacerbation, as it is highly likely that the normal flora will have been influenced by antibiotic exposure and they may have infection due to organisms resistant to first line agents.

2d Pneumonia (Community acquired)

In pneumonia antibiotics are clearly beneficial.

Assess the CRB-65 score for all people diagnosed with pneumonia:

One point is awarded for each of the following features:

- Confusion - recent
- Respiratory rate 30 breaths/min or greater
- Blood pressure - systolic of 90 mmHg or less or a diastolic of 60 mmHg or less
- 65 years of age or older

For people with a CRB-65 score of 3 or more, arrange urgent admission to hospital.

For people with a CRB-65 score of 2, arrange same-day assessment in secondary care. Secondary care options include short-stay inpatient treatment or hospital-supervised outpatient treatment.

For people with a CRB-65 score of 1, consider arranging same-day assessment in secondary care. For people with a CRB-65 score of 0, treatment at home is usually appropriate, depending on clinical judgement and available social support.

Give immediate IM benzylpenicillin or amoxicillin 1g PO if delayed admission life threatening.

First line:

Amoxicillin 500mg to 1g tds for 7 to 10 days
Or

Doxycycline 200mg stat then 100mg od for 7 to 10 days

(If known history of MRSA or high suspicion of MRSA or if allergic to penicillin)

Severe infection (that would normally be treated in hospital but if admission not possible):

Amoxicillin 1g tds in combination with clarithromycin 500mg bd for 7 to 10 days

Treatment failure:

Levofloxacin 500mg od for 10 to 14 days
Levofloxacin would not routinely be used in the context of community acquired pneumonia but may be considered in exceptional circumstances e.g. patients not responding to amoxicillin in combination with clarithromycin or patients with known carriage of resistant organisms.

If atypical pneumonia (e.g. mycoplasma infection) is suspected use both of the above first line agents (amoxicillin and clarithromycin) and continue for 14 days in total.

If post-influenza or post chickenpox:

Add fludoxacin 500mg qds for 10 days to either amoxicillin or clarithromycin.

General Note:

- For more information regarding IV therapy then please see page 3 and Appendix 2.
- For further information regarding long term antibiotic prophylaxis in adults then please see page 4.

2e Infected Exacerbation of bronchiectasis

A freshly collected sputum sample should be taken and treatment must be started on the basis of microbiological results.

If Pseudomonas aeruginosa has NOT been previously isolated then:

Co-amoxiclav 625mg tds for 7 days

For those patients known to be carrying Pseudomonas aeruginosa (as long as the isolate remains quinolone sensitive) then use:

Ciprofloxacin 750mg bd for 7 days

For empiric treatment outside of these scenarios then seek advice from Microbiology.

3 URINARY TRACT INFECTIONS (UTI)

MRSA

MRSA is typically resistant to many broad spectrum agents such as macrolide and quinolone antibiotics. Prescribing of inappropriate broad spectrum agents in patients colonised by MRSA disrupts the patient's normal flora and allows MRSA to increase in numbers. This renders the patient more vulnerable to (potentially severe) MRSA infection.

It is therefore of great importance to be aware of previous MRSA results prior to prescribing.
Notes:
- For all UTIs encourage adequate fluid intake.
- Use simple generic antibiotics first line whenever possible.
- Avoid broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) when narrow spectrum antibiotics remain effective as they increase risk of Clostridium difficile, MRSA and resistant UTIs. (Health Protection Agency - www.hpa.org.uk)
- For more information regarding IV therapy then please see page 3 and Appendix 2.
- For further information regarding long term antibiotic prophylaxis in adults then please see page 4.

3a  Uncomplicated Acute Cystitis in Non Pregnant Women <60 years
Specimens are not required for 'one-off' infections in previously healthy women.

First line:
- Trimethoprim 200mg bd for 3 days
- Nitrofurantoin 50mg qds or 100mg MR bd for 3 days

Treatment failures:
If culture available, treat according to sensitivity results.
If not, obtain specimen for culture and sensitivity first and then prescribe:
- Co-amoxiclav 375mg tds for 3 days
- Ciprofloxacin 250mg bd for 3 days

Review when microbiology results available.

Notes:
- Nitrofurantoin should be taken with food.
- Nitrofurantoin is contra-indicated if CrCl <60ml/min.
- Both immediate and modified-release formulations of nitrofurantoin are recommended because there is no evidence to prefer one over the other.

3b Acute Cystitis in Women >60 years, Men and Other Complicated Infections
Obtain specimen before empirical treatment. Specimens from women are not infrequently contaminated so thorough vulval cleansing prior to collection must be stressed.

The definition of a complicated UTI is a UTI when one or more factors are present that predispose the person to persistent infection, recurrent infection or treatment failure. Examples include UTI with:
- Abnormal urinary tract (for example calculus, vesicoureteric reflux, reflux nephropathy, neurogenic bladder, indwelling catheter, urinary obstruction, recent instrumentation).
- Impaired host defences (for example poorly controlled diabetes mellitus, immunosuppressive treatment).
- Impaired renal function.

Note:
Asymptomatic bacteriuria in the elderly should not generally be treated.

It may be appropriate to prescribe a 3 day course of antibiotics for women >60 years, providing there are no complicating factors or latent urological problems.¹

First line:
1. Trimethoprim 200mg bd for 7 days
or
2. Nitrofurantoin 50mg qds or 100mg MR bd for 7 days
   (Not in the elderly >70 years due to side effects profile)
or
3. Cefalexin 500mg bd or tds for 7 days (depending on severity)

Treatment failures:
If culture available, treat according to sensitivity results.
If not, obtain specimen for culture and sensitivity first and then prescribe:
- Co-amoxiclav 375mg tds for 7 days
- Ciprofloxacin 250mg bd for 7 days

Review when microbiology results available.

Investigations in Adults

Uses and Limitations of Urine Dipstick Tests

<table>
<thead>
<tr>
<th>Test Result</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrite</td>
<td>Most urinary pathogens reduce nitrate to nitrite, and a positive test is suggestive of bacteriuria. A negative test does not rule out UTI, because some pathogens do not produce nitrate reductase, and frequent urination (which is common in cystitis) gives the enzyme less time to react.</td>
</tr>
<tr>
<td></td>
<td>If the dipstick is exposed to air, the nitrite test can become inactive.</td>
</tr>
<tr>
<td>Leucocyte esterase (LE)</td>
<td>LE is a marker for leucocytes (i.e. pyuria) but the LE test is less sensitive than microscopy.</td>
</tr>
<tr>
<td></td>
<td>A positive LE test indicated pyuria and therefore suggests UTI, but leucocytes can contaminate the specimen, so a positive test does not make a diagnosis of UTI certain.</td>
</tr>
<tr>
<td></td>
<td>A negative LE test does not rule out the diagnosis of UTI, because the test is insensitive and pyuria is not always found in UTI.</td>
</tr>
<tr>
<td>Blood and protein</td>
<td>Blood and protein are sometimes found in the urine when there is a UTI, but neither their presence nor their absence helps in making a diagnosis of UTI.</td>
</tr>
<tr>
<td>Combination of tests</td>
<td>In adult patients it is reasonable to exclude UTI if both nitrite and LE dipstick tests are negative.</td>
</tr>
<tr>
<td>In otherwise healthy women</td>
<td></td>
</tr>
<tr>
<td>with urinary symptoms:</td>
<td></td>
</tr>
<tr>
<td>If the dipstick is positive</td>
<td></td>
</tr>
<tr>
<td>nitrite and/or leucocyte esterase, also culture the urine, unless it is the first presentation. If the dipstick is negative, do not culture the urine. Culture the urine to support decisions made on dipstick test results.</td>
<td></td>
</tr>
<tr>
<td>In men, urine should be cultured whenever a urinary tract infection is suspected (even if dipstick tests are negative).</td>
<td></td>
</tr>
<tr>
<td>Urine dipstick tests are not suitable for screening for UTI in asymptomatic men.</td>
<td></td>
</tr>
</tbody>
</table>
For infants and children 3 months or older with cystitis / lower urinary tract infection:
- Treat fever and pain with paracetamol. NSAIDs should be avoided.
- Treat with oral antibiotics for 3 days
  
  **First line:**
  - Trimethoprim
  - Nitrofurantoin
  - Cefalexin

  **Treatment failures:**
  Guided by microbiology results.

(For appropriate paediatric doses see page 34 to 35)

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**Investigations in Children:**
For information regarding investigations in children with UTI then please visit:
www.wirral.mapofmedicine.com
www.nice.org.uk/guidance/CG54
If required, seek specialist guidance from the Department of Paediatrics, Arrowe Park Hospital.

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**Collection / Storage for Women, Men and Children**
- Careful collection, storage and transport of urine samples minimises contamination and deterioration.
- The urine sample should be collected, if possible, before antimicrobials are taken or changed.
- A clean catch mid-stream urine sample (MSU) is recommended.

**Women:**
- The perineum should be wiped from front to back with a gauze swab moistened with water (antiseptics should be avoided because they may inhibit bacterial culture). A wide mouthed gailipot or disposable funnel facilitates collecting an MSU. Women who are menstruating must take particular care to avoid contamination.

**Men:**
- Procedure:
  - Withdraw prepuce and clean glans penis.
  - Discard the first portion of urine and catch the middle portion (a wide mouthed gailipot or disposable funnel is useful).

**Children:**
- In infants, urine can be collected from an absorbent pad in the nappy. Alternatively the clean catch method or an adhesive bag can be used.
- In toddlers, a potty is convenient. The potty should be cleaned with detergent and hot water (bleach should not be used because it may inhibit culture of bacteria).
- In older children, a clean catch MSU can be collected with little difficulty and is adequate for diagnosis.

**Containers** - urine should be transferred within thirty minutes of collection to a specimen bottle.
**Storage** - urine should be refrigerated at 4°C while waiting to be processed. Urine that has been stored at 4°C for 48 hours is suitable for culture but not for microscopy as many cells would have disintegrated.
Admission is required for patients who are:
- Significantly dehydrated or who are unable to take oral fluids and medications.
- Have signs of sepsis.
- Pregnant and pyrexial.

Consider admitting people who are able to take oral fluids and medications if they are pyrexial and have a risk factor for developing a complication. Have a low threshold for admission or hospital assessment for patients with:
- Immunocompromise.
- A foreign body in the renal tract.
- Abnormalities of the renal tract anatomy or function.
- Diabetes.
- Renal impairment.
- Advancing age.

Always obtain a specimen before starting empirical treatment of:

Cefalexin 500mg bd for 7 days
or
Co-amoxiclav 625mg tds for 14 days. This could be considered as an alternative for those patients unable to receive ciprofloxacin e.g. epileptic or previous tendonitis.

In pregnancy, if admission to hospital is not required:
Cefalexin 500mg bd for 10 to 14 days
Review microbiology results and consider urological referral if no response to treatment within 48 hours.

If faecal streptococci are isolated then amoxicillin is the preferred choice (in cases where the organism is sensitive):
Amoxicillin 500mg tds for 14 days

Choice of antibiotic depends on activity against the likely pathogens and prostatic tissue penetration. An MSU taken prior to therapy should identify the organism but will not localise infection to the prostate.
Trimethoprim 200mg bd for 28 days
(High concentrations in prostatic fluid and inexpensive)
or
Ciprofloxacin 500mg bd for 28 days
(Broader activity but more expensive)

Notes:
- Refer patients with chronic prostatitis to Urologists.
- Repeat urine culture one week after completion of antibiotic course to ensure infection resolved.

Infection Associated with Indwelling Urinary Catheters
There is a high incidence of bacteriuria with long term catheters. Antibiotics do not eliminate these, but lead to the growth of resistant organisms. Culture of urine is not normally advised. Fluid intake must be encouraged.

Where there is systemic infection and an antibiotic needs to be prescribed, it may be of value to change the catheter while the patient is receiving therapy.
Blocked catheters may need to be changed. Bladder washouts require nothing stronger than normal saline. Chlorhexidine washouts are not thought to be helpful and may cause bladder irritation and haematuria.

Consider prophylactic antibiotics at the time of catheter change for patients who:
- have a history of symptomatic urinary tract infection after catheter change
or
- have experienced frank haematuria after catheterisation
or
- have required two or more attempts of catheterisation

No antibiotic is licensed for single dose or short course prophylaxis of urinary tract infections when changing long-term urinary catheter. It is important to fully inform patients about the advantages and disadvantages of using antibiotics for their individual circumstances, and the importance of fully adhering to the antibiotic prophylaxis regimen to reduce the risk of bacterial resistance. Patients should be asked their preference and to consent on the antibiotic prophylaxis prescribed.

Additional guidance will be available in the near future.

Epididymo-orchitis
In adolescents and men younger than 35 years of age, epididymitis and epididymo-orchitis are usually caused by sexually transmitted infections (Chlamydia trachomatis or Neisseria gonorrhoeae). In the context of likely sexual acquisition then referral to Contraception & Sexual Health Clinics or to GUM is imperative.

In men aged 35 years or older, epididymitis and epididymo-orchitis are usually caused by enteric organisms that cause urinary tract infections (when they are often in association with anatomical abnormalities of the urinary tract). Outside of sexual acquisition then use:

Trime thoprim 200mg bd for 10 days
or
Ciprofloxacin 500mg bd for 10 days

Skin and Soft Tissue Infections

MRSA and PVL-SA:
MRSA is typically resistant to many broad spectrum agents such as macrolide and quinolone antibiotics. Prescribing of inappropriate broad spectrum agents in patients colonised by MRSA disrupts the patient’s normal flora and allows MRSA to increase in numbers. This renders the patient more vulnerable to (potentially severe) MRSA infection. It is therefore of great importance to be aware of previous MRSA results prior to prescribing.

4c. Skin and Soft Tissue Infections

**Mild infection**
- Flucloxacillin 500mg qds for 7 days
  - or
- Clarithromycin 250 to 500mg bd for 7 days
  (If allergic to penicillin)

**More severe infections (such as cellulitis)**
- Flucloxacillin 500mg qds for 7 to 14 days
  (High dose flucloxacillin also gives cover against Group A Streptococci)
  - or
- Clarithromycin 500mg bd for 7 to 14 days
  (If allergic to penicillin)

**Facial cellulitis**
- Co-amoxiclav 500/125mg tds for 7 to 14 days
  - or
- If river or sea water exposure, discuss with microbiologist

Important Note:
- Co-amoxiclav may be considered as a first line agent if the cellulitis is associated with a long term ulcer or pressure sore.
- Co-amoxiclav exerts a considerably broader spectrum of activity including Gram-negative organisms and anaerobes which is usually unnecessary in the treatment of cellulitis.

Notes:
- 'Routine' swabs are not required from leg ulcers and should only be taken when there is a clear clinical indication. Antibiotics are only recommended if cellulitis is associated with the leg ulcer when the treatment regimen above for “More severe infections” should be used. Lower limb cellulitis may take up to 14 days to respond. Elevation of the limb may speed response.
- Severe cellulitis in patients with underlying pathology such as lymphoedema may require prolonged therapy of several weeks duration.
- Topical antibiotics should be reserved for very localised lesions. Monotherapy with topical treatments such as fusidic acid should be avoided when treating skin and soft tissue infections such as impetigo as resistance may develop to fusidic acid.
- Swabs are required for PEG site infections. Treatment should be provided accordingly.

4d. Infected Diabetic Foot Ulcer

Referral to the Diabetic Foot Ulcer Clinic is essential as per the Diabetic Foot Ulcer Outpatient Pathway.

For superficial infection flucloxacillin may be considered for initial management - in all other cases expert opinion is required.

4e. Mastitis

**Suspect infectious mastitis if:**
- Symptoms are severe from the beginning.
- A nipple fissure is visible.
- Symptoms do not improve after 12 to 24 hours despite effective milk removal.
- Bacterial culture is positive.

**Empirical treatment is:**
- Flucloxacillin 500mg qds for 7 to 14 days
  - or
- Clarithromycin 250 to 500mg bd for 7 to 14 days
  (If allergic to penicillin)

Advise the woman to continue to breastfeed. These antibiotics are only excreted in milk in very small amounts. Usually the infant is not affected, but occasionally stools may be looser or more frequent than usual or the infant may be more irritable.

**If the results of breast milk culture are available**, prescribe an antibiotic according to the sensitivities of the organism that has been identified.

4d. Human/Animal Bites

**Antibiotics are not generally needed if the wound is 3 or more days old and there is no sign of local or systemic infection.**

i. Human bites:

**Prophylaxis**
- Prescribe prophylactic antibiotics for all human bite wounds under 72 hours old, even if there is no sign of infection.
  - Co-amoxiclav 375mg tds for 7 days
  - or
  - Metronidazole 400mg tds plus doxycycline 100mg bd for a minimum of 7 days
    (If allergic to penicillin)
  - Reassess at 24 & 48 hours after starting course of antibiotic treatment
  - or
  - Metronidazole 400mg tds plus clarithromycin 500mg bd for 7 days
    (If allergic to penicillin)
  - Reassess at 24 & 48 hours after starting course of antibiotic treatment

**TREATMENT**
- Co-amoxiclav 625mg tds for a minimum of 7 days
  - or
  - Metronidazole 400mg tds plus doxycycline 100mg bd for a minimum of 7 days
    (If allergic to penicillin)
  - Reassess at 24 & 48 hours after starting course of antibiotic treatment
  - or
  - Metronidazole 400mg tds plus clarithromycin 500mg bd for a minimum of 7 days
    (If allergic to penicillin)
  - Reassess at 24 & 48 hours after starting course of antibiotic treatment

In the context of human bites all patients should be reviewed for HIV Post Exposure Prophylaxis (PEP) and Hepatitis B prophylaxis. Consider if tetanus prophylaxis is appropriate.

ii. Animal bites:

**Prescribe antibiotics for:**
- All cat bites, animal bites to the hand, foot, and face, puncture wounds, wounds requiring surgical debridement, wounds involving joints, tendons, ligaments, or suspected fractures.
- Wounds that have undergone primary closure.
- People who are at risk of serious wound infection (e.g. those who are diabetic, cirrhotic, asplenic, or immunosuppressed).
- People with a prosthetic valve or a prosthetic joint.
Prophylaxis
Co-amoxiclav 375mg tds for 7 days
or
Metronidazole 400mg tds plus doxycycline 100mg bd for 7 days
(if allergic to penicillin)
Reassess at 24 & 48 hours after starting course of antibiotic treatment

Treatment
Co-amoxiclav 625mg tds for a minimum of 7 days
or
Metronidazole 400mg tds plus doxycycline 100mg bd for a minimum of 7 days
(if allergic to penicillin)
Reassess at 24 & 48 hours after starting course of antibiotic treatment
or
Azithromycin for 3 days plus metronidazole for a minimum of 7 days
(in penicillin allergy in children)
Reassess at 24 & 48 hours after starting course of antibiotic treatment

In the context of animal bites then assess the risk of acquiring rabies, and discuss the need for post-exposure prophylaxis urgently with the Virus Reference Department of the Health Protection Agency (telephone 020 8327 6017).

Note:
Erythromycin should never be used alone in prophylaxis or treatment of animal bite wounds. More than 80% of P. multocida are resistant and serious clinical failures including meningitis have been documented following erythromycin treatment.

4e MRSA Decolonisation in Colonised Patients

Notes:
- Methicillin-Resistant Staphylococcus aureus (MRSA) is a variety of Staphylococcus aureus that has developed resistance to a number of common antibiotics.
- It is usually commensal, neither harming nor benefiting the host.
- MRSA colonisation occurs when people carry MRSA on their skin or in the gut or nose but do not show symptoms and signs of infection.
- MRSA infection occurs when MRSA causes harm by entering the tissues for example through a cut or wound and requires treatment.
- Spread can be prevented through regular hand washing.
For further information please see Infection Control Guidance at http://www.wirralct.nhs.uk/index.php/our-services/services/infection-prevention-and-control

Octenisan® is the antiseptic MRSA decolonisation product of choice.

i) Prior to admission for elective procedures patients will be tested for MRSA. For those patients with positive results, GPs will be asked to prescribe decolonisation therapy as follows:
- Octenisan® body wash 150ml (a 500ml bottle is available for larger patients). Apply daily for 5 days.
- Mupirocin 2% nasal ointment 3g. Apply tds to both nostrils for 5 days.
Eradicative treatment should be commenced 7 days prior to admission.

ii) For all other patients identified as MRSA positive, the MRSA Decolonisation Guidance should be followed, which can be found at the following web address:
The MRSA Decolonisation Risk Assessment Tool must be completed to determine if decolonisation therapy is necessary.

Note:
Naseptin should NOT be routinely used for MRSA decolonisation. This is to be reserved for cases of mupirocin resistance only.

Method and instructions for the use of Octenisan®
Bath, wash or shower with Octenisan® body wash for a total of 5 days.
- Wet skin and/or hair.
- Apply an adequate amount of undiluted Octenisan® body wash onto a clean washcloth.
- Wash the whole body and/or hair, paying particular attention to moist, hairy areas including armpits, belly button, groin and perineum.
- Hair should be washed at least twice a week or upon every hair wash.
- After 1 minute, the wash may be rinsed off.
- Dry with a clean towel and dress in clean clothing.
If bathing, do not pour Octenisan® into the bath/wash water as the correct dilution will not be achieved.

Method and instructions for the use of Mupirocin Nasal Ointment
- Squeeze out a thin line of ointment about 1cm long.
- Apply ointment to the inside of the nostril and then repeat for the other nostril.
- Close nostrils by pressing the sides of the nose together for a moment - this ensures that the ointment is spread inside each nostril.
- Remain seated for 5 minutes after application to ensure the ointment trickles to the back of the nose and throat - you should taste the ointment at the back of your throat.
- Hands should be washed.

4f Dental Abscess
A dental practitioner should provide definitive treatment of a dental abscess. Antibiotics should only be prescribed for patients who are systematically unwell, if there are signs of severe infection or for high risk patients to reduce the risk of complications (e.g. the people who are immunocompromised, diabetic or have valvular heart disease). If emergency dental care is unavailable, a 5 day course of the following antibiotics could reasonably be prescribed:
- Amoxicillin or metronidazole (or clarithromycin if neither are suitable).

4g Acne Vulgaris

4h Rosacea

4i Scabies

4j Treatment of Cutaneous Fungal Infections
For treatment guidance for 4g, 4h, 4i and 4j please refer to the Wirral Formulary.
The Wirral Formulary can be found at the following web address:
http://mm.wirral.nhs.uk/formulary/
5 EYES

5. Conjunctivitis

Management Strategies

Treat if severe, as most viral or self-limiting4.

A study was undertaken of 307 adults and children (aged 1 year or more) with uncomplicated acute infective conjunctivitis. The patients were assigned to receive immediate antibiotic treatment, delayed antibiotic treatment (prescription to be collected after 3 days if considered necessary) or no antibiotic therapy. Antibiotic treatment was with topical chloramphenicol.

Prescribing strategies did not affect the severity of symptoms but duration of moderate symptoms was less with antibiotics (no antibiotics - 4.8 days duration, delayed antibiotics - 3.9 days duration and immediate antibiotics - 3.3 days duration).

The authors concluded that delayed prescribing of antibiotics is probably the most appropriate strategy for managing acute conjunctivitis in primary care4.

Adults and Children

First line:
- Chloramphenicol 0.5% eye drops, use 1 drop every 2 hours for 2 days, then every 4 hours (whilst awake) AND 1% ointment at night

Notes:
- Gentamicin 0.3% eye drops could be considered as an alternative to chloramphenicol.
- Fusidic acid 1% eye drops are more expensive than chloramphenicol eye drops but only need to be applied twice daily. They should be considered for:
  - Patients who are pregnant.
  - School children or those who require a carer to administer eye drops.

Remember:
Continue treating for a further 48 hours after signs and symptoms have been resolved.
Consider using delayed antibiotic prescriptions where appropriate.

Neonates

As per Adults and Children above.
Take a swab for Chlamydia if failure to respond. Ophthalmia neonatorum is a reportable disease and should be reported to the Consultant in Health Protection.

5.2 Blepharitis

Cleansing of the eyelids can be carried out using a variety of agents (e.g. baby shampoo diluted with warm water).
Cleansing of the eyelids should be done twice daily initially. Once symptoms have improved this can be reduced to once daily. Daily cleansing should be continued indefinitely in order to reduce the likelihood of recurrence.
Topical antibiotics e.g. chloramphenicol 1% ointment (an alternative is fusidic acid 1% eye drops) should only be used if there is marked eyelid infection. They should be rubbed into the eyelid margin using a fingertip or cotton bud. This is to be carried out after cleansing the eyelid.

Note:
Treat for 4 to 6 weeks. Topical antibiotics are not recommended for long-term use.

6 SEXUAL HEALTH

Gonococcal and chlamydial infections are diagnosed by nucleic acid amplification techniques (NAATS). Samples used are:
- Endocervical / urethral / throat and rectal swabs.
- Urine sample.
- Self taken swab (women only).
Swabs for culture to enable antibiotic sensitivity to be established are always advised if a NAATS test is positive for gonorrhoea. All patients with positive NAATS for gonorrhoea should be referred to GUM clinic in Arrowe Park for further management.

Trichomonas infection may be diagnosed from a high vaginal swab (HVS). Candidiasis and bacterial vaginosis (BV) are usually diagnosed in the light of clinical symptoms; however a HVS is usually needed for microscopy to confirm the diagnosis. Cases of recurrent BV need further review and should be referred to the GUM clinic.

In the case of a sexually transmitted infection, contacts will need to be traced and treated.
Attendance at Contraception & Sexual Health Clinics (CASH) or referral to Genito-Urinary Medicine (GUM) or Department of Obstetrics & Gynaecology may be appropriate.

6.6 Vulvovaginal Candidiasis

Clotrimazole vaginal preparations - a single dose of 500mg at night is as effective as a lower dose divided over several days.
Fluconazole - 150mg stat orally.

Note:
Fluconazole may be used first line as long as there are no azole interactions or contra-indications.

Pregnancy:
- Use longer courses of topical clotrimazole (about 7 days or more) in pregnancy. Oral antifungal therapy should be avoided. If a pessary is used in pregnancy, then women should be advised not to use the applicator.
- Topical miconazole is a suitable alternative.

Recurrent Vulvovaginal Candidiasis

Recurrent vulvovaginal candidiasis occurs in less than 5% of women. It is defined as:
- FOUR or more episodes of symptomatic vulvovaginal candidiasis in 1 year (with at least partial resolution of symptoms between episodes) AND
- Proven diagnosis with HVS culture on at least TWO occasions when symptomatic
Pre-disposing risk factors should be eliminated or controlled as much as possible (uncontrolled diabetes, immunosuppression, frequent antibiotic use).

In cases of recurrent vulvovaginal candidias it may be useful to ask the laboratory to formally identify the Candida species as non-albicans Candida may not respond to treatment with fluconazole.4
Referral to Genito-Urinary Medicine (GUM) or Department of Obstetrics & Gynaecology may be appropriate e.g. in non-albicans Candida species infections, pregnancy (or risk of), breastfeeding, girls <16 years or if treatment with oral fluconazole unsuitable or contra-indicated.

An induction regimen to ensure clinical remission
Fluconazole 150mg every 72 hours x 3 doses (off-label)
Followed immediately by maintenance regimen
Fluconazole 150mg once a week for 6 months (off-label)
or
Clotrimazole pessary 500mg once a week
Oral antifungal therapy should be avoided in pregnancy/risk of pregnancy and breastfeeding.

Topical treatments (if a woman prefers topical treatment or cannot tolerate oral metronidazole)

Fluconazole 150mg bd for 5-7 days
(Topical clindamycin may not prevent late ulcerations and skin rashes) should be referred to GUM for further management.

Notes:
- Avoiding high dose (2g) regimen in pregnancy and breast feeding.
- Topical clindamycin is safe to use in pregnancy, (however, the manufacturers advise caution in the first trimester due to a lack of safety data). Treatment with topical clindamycin may not prevent the above complications.

Bacterial Vaginosis

Oral treatment:
Metronidazole 400mg bd for 5-7 days
(Metronidazole 2g as a single oral dose may be considered as an alternative if adherence is an issue).
Topical treatments (if a woman prefers topical treatment or cannot tolerate oral metronidazole) include:
- Intravaginal clindamycin cream 2% once a day at night for 7 days
- Intravaginal metronidazole gel 0.75% once a day at night for 5 days

Notes:
Bacterial vaginosis during pregnancy is associated with late miscarriage, premature rupture of membranes, pre-term birth and post-partum endometritis.
Offer treatment to all pregnant women who are symptomatic.
Although evidence suggests that metronidazole is safe in pregnancy and is not teratogenic, the high dose (2g) regimen must be avoided (as advised by the manufacturers).
Topical clindamycin is safe to use in pregnancy, (however, the manufacturers advise caution in the first trimester due to a lack of safety data). Treatment with topical clindamycin may not prevent the above complications.

Gonorrhoea

Referral to GUM is recommended or Contraception and Health Clinics (CASH).
Counselling, testing for other infections and partner notification are integral to patient management.

Pelvic Inflammatory Disease

Referral to GUM or Contraception and Health Clinics (CASH) is recommended.
Usual causes are Chlamydia trachomatis and/or Gonorrhoea neisseria and genital mycoplasmas.
Counselling, testing for infections and partner notification are integral to patient management.
Rest, analgesia and review required.

Syphilis

There have been outbreaks of Syphilis in North West. All suspected cases of Syphilis (genital/oral ulcerations and skin rashes) should be referred to GUM for further management.
6j. Genital Ulcers
Usually presents as acute painful genital ulcerations.
Treatment:
- Aciclovir 200mg five times a day for 5 days
- Aciclovir 400mg three times a day for 5 days
Referral to GUM may be required.

6k. Genital Warts / Human Papilloma Virus (HPV) Infection
Treatment varies as per clinical presentation. Follow up reviews are required to monitor therapy hence referral to GUM may be helpful.

7. GASTROENTERITIS
Fluid replacement is essential. Antibiotic therapy is not usually indicated. Many cases are viral in origin and even in bacterial gastroenteritis, antibiotics reduce diarrhoea by only 1 to 2 days. Initiate treatment on the advice of the microbiologist if the patient is systematically unwell.

Specimens should be taken in:
- All cases of bloody diarrhoea.
- Patients who are systemically unwell.
- Travellers from abroad.
- Food handlers.
- In cases with persistent symptoms (e.g. duration of 7 days or longer).

The threshold for investigation should be lower in young children and elderly frail patients (e.g. 3 or more days duration).

Workers (including food handlers) can normally return to their duties when they have been symptom free for 48 hours. In certain rare instances (e.g. infection with E. coli 0157) exclusion from work/school/nursery may be required. In these situations you will be contacted by Medical Microbiology and/or Health Protection Agency. Similarly clearance cultures are only rarely required on Public Health grounds.¹

Notes:
- Food poisoning should be notified to the Consultant in Health Protection. For the local contact, please telephone 0844 225 1255 (daytime 9am to 5pm).
- For further details please go to the Health Protection Agency website - www.hpa.org.uk

7b. Campylobacter Enteritis
(notifiable to Consultant in Health Protection)
Antibiotic treatment is not usually indicated. Initiate on the advice of Medical Microbiology if the patient is systemically unwell.

7c. Cryptosporidium
(notifiable to Consultant in Health Protection)
There is no effective treatment available. Symptoms may take 2 to 3 weeks to resolve. Transmission from person to person is commonplace so strict hygiene measures must be followed.

7d. Salmonellosis
(notifiable to Consultant in Health Protection)
Antibiotic treatment not usually indicated. Initiate on the advice of Medical Microbiology if the patient is systemically unwell.

7e. Clostridium difficile infection - CDI

Notes:
- C. difficile is a bacterium present in the gut flora of some people.
- Antimicrobials disturb the balance of the gut flora allowing C. difficile to multiply and cause infection.
- Symptoms of C. difficile can vary from mild diarrhea to fatal bowel inflammation.
- C. difficile spores are shed in the faeces. The spores can survive for long periods in the environment.
- CDI has commonly been associated with hospital stay but it is being recognised that many cases originate in the community.
- Patients most at risk include:
  - Elderly.
  - Suffering from severe underlying diseases.
  - Immunocompromised.
  - In an environment where they are in close contact with one another.
- Other factors that increase the risk of CDI are:
  - Use of antimicrobials.
  - Cytotoxic chemotherapy.
  - Recent gastrointestinal procedures.
  - Presence of a nasogastric tube.
  - The use of Proton Pump Inhibitors (PPIs) might increase the risk of CDI.

7f. Acute Diarrhoea and Vomiting
Usually viral and self-limiting. Antibiotics only tend to prolong the carrier state, do not shorten the duration of the illness and may be contraindicated. Antibiotics should only be commenced on the advice of Medical Microbiology.

Oral rehydration therapy is the mainstay of treatment.
Mild cases may respond to withdrawal of the predisposing antibiotic(s) and/or stopping of any Proton Pump Inhibitors if unnecessary.

Manage fluid loss.

Otherwise for mild to moderate CDI:
Metronidazole 400mg tds for 10 days for confirmed Clostridium difficile toxin positive diarrhoea.
A recurrent attack should be treated with a further course of metronidazole.

Patients with severe symptoms or who are not responding to oral metronidazole after 5 days of therapy should be considered for secondary care admission and/or oral vancomycin therapy (for 10 to 14 days). Seek further advice from Medical Microbiology.

Notes:
- Requires test of stool sample for the presence of Clostridium difficile toxin.
- May occur up to four weeks or even longer after antibiotic treatment.
- It is not necessary to send repeat stool samples after therapy has finished, as stool samples frequently remain toxin positive even in patients who are symptom free.
- Patients who have had previous Clostridium difficile infection remain vulnerable to recurrence or re-infection if further courses of broad-spectrum antibiotics are used.
- Consider stopping unnecessary PPI therapy in patients at higher risk or with Clostridium difficile infection.

Consider ‘blind’ treatment of family contacts.

7j Giardia Lamblia
(notifiable to Consultant in Health Protection)
Adults:
Metronidazole 400mg tds for 5 days or 2g once daily for 3 days.

Children:
1 to 3 years 500mg once daily for 3 days
3 to 7 years 600 to 800mg once daily for 3 days
7 to 10 years 1g once daily for 3 days
Over 10 years as per adult dose

7g Acute Cholecystitis
Analgesia should be provided. Referral may be appropriate.
In patients with raised temperature, co-amoxiclav 625mg tds for 5 days may be prescribed.

7h Acute Diverticulitis
Referral may be appropriate. Consider using:
- Co-amoxiclav 625mg tds for at least 5 days
- Ciprofloxacin 500mg bd plus metronidazole 400mg tds for at least 5 days
  (if allergic to penicillin)

8 CENTRAL NERVOUS SYSTEM INFECTIONS
Probable Bacterial Meningitis / Meningococcal Septicaemia

Do not give antibiotics if this would delay urgent transfer to hospital. 

Community Pre-Admission Treatment: Cefotaxime (single dose)

Neonate or children - 50mg/kg (maximum 1g) stat IV or IM
Adults - 1g stat IV or IM

Note:
Cefotaxime is the most effective choice in terms of spectrum of activity (including penicillin resistant pneumococci). However benzylpenicillin would also be appropriate to use in an emergency situation or where there is a high index of suspicion regarding meningococcal aetiology.

Community Pre-Admission Treatment: Benzylpenicillin (single dose)
Children <1 year 300mg stat IV or IM
Children 1 to 9 years 600mg stat IV or IM
Adults and children over 10 years 1.2g stat IV or IM

Control of Meningococcal Disease
GP to liaise with Consultant in Health Protection (Daytime Tel (9am to 5pm): 0844 225 1295, Infection Control Team, Public Health and HPA with regards to arranging community control measures (e.g. prescriptions for antibiotic prophylaxis for close contacts).
For out of hours services (after 5pm) contact Public Health on call through the Royal Liverpool and Broadgreen University Hospitals NHS Trust switchboard on 0151 706 2000.
For more information go to www.hpa.org.uk

9 VIRAL INFECTIONS

9a Herpes Zoster (Shingles)
Aciclovir 800mg five times daily for 7 days

Clinical value minimal unless started within 72 hours of onset of rash.
A course of famciclovir 750mg tablets costs significantly more than a course of aciclovir dispersible 800mg. It is not recommended for routine use.

9b Varicella (Chickenpox)
Offer symptomatic treatment.
For adults, consider prescribing aciclovir 800mg five times a day for 7 days if they present within 24 hours of the onset of the rash (particularly if severe chickenpox or risk of complications).
For children, aciclovir is not recommended in chickenpox.

10 PARASITE INFECTIONS

Threadworm
Children over 6 months or adults:
Mebendazole 100mg as a single dose.
If re-infection occurs, a second dose may be needed two weeks later.
11 ANTIBIOTIC PROPHYLAXIS

11a Antibiotic Prophylaxis against Infective Endocarditis

NICE GUIDANCE

Antibacterial prophylaxis and chlorhexidine mouthwash are not recommended for the prevention of endocarditis in patients undergoing dental procedures.

Patients at risk of endocarditis include:

- Acquired valvular heart disease with stenosis or regurgitation.
- Valve replacement.
- Structural congenital heart disease.
- Previous infective endocarditis.
- Hypertrophic cardiomyopathy.

Antibiotic prophylaxis is not recommended for the prevention of endocarditis in patients undergoing procedures of the:

- Upper and lower respiratory tract (including ear, nose and throat procedures and bronchoscopy).
- Genito-urinary tract (including urological, gynaecological and obstetric procedures).
- Upper and lower gastrointestinal tract.

Any infection in patients at risk of endocarditis should be investigated promptly and treated appropriately to reduce the risk of endocarditis.

If patients at risk of endocarditis are undergoing a gastrointestinal or genito-urinary tract procedure at a site where infection is suspected, they should receive appropriate antibacterial therapy that includes cover against organisms that cause endocarditis.

Patients at risk of endocarditis should be:

- Advised to maintain good oral hygiene.
- Told how to recognise the signs of infective endocarditis, and advised when to seek expert advice.

For further information: www.nice.org.uk/C64

11c Management of Splenectomy Patients

Patients who suffer with asplenia or hyposplenia (including homozygous sickle cell disease and coeliac syndrome) are at increased risk of overwhelming bacterial infection. Infection is most commonly pneumococcal but other organisms such as Haemophilus influenzae type b and meningococci may be involved.

The risk is greatest in the first 2 years following splenectomy and is greater amongst children, but persists into adult life.

Refer to Immunisation Against Infectious Disease - ‘The Green Book’ Chapter 7 for up-to-date vaccination requirements - available at: http://immunisation.dh.gov.uk/gb-complete-current-edition/

Lifelong antibiotic prophylaxis is required in all cases. Phenoxymethylpenicillin (penicillin V) is preferred unless cover is also needed against Haemophilus influenzae for a child at least up to 16 years (in which case, give amoxicillin) or if the patient is allergic to penicillin (in which case, give erythromycin).

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenoxymethylpenicillin</td>
<td>Child &lt; 1 year</td>
<td>62.5mg bd</td>
</tr>
<tr>
<td>(Penicillin V)</td>
<td>Child 1 to 5 years</td>
<td>125mg bd</td>
</tr>
<tr>
<td></td>
<td>&gt; 5 years and adults</td>
<td>250mg bd</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Child 1 month to 5 years</td>
<td>125mg bd</td>
</tr>
<tr>
<td></td>
<td>Child 5 to 12 years</td>
<td>250mg bd</td>
</tr>
<tr>
<td></td>
<td>Child 12 to 18 years</td>
<td>500mg bd</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Child 1 month to 2 years</td>
<td>125mg bd</td>
</tr>
<tr>
<td></td>
<td>Child 2 to 8 years</td>
<td>250mg bd</td>
</tr>
<tr>
<td></td>
<td>&gt; 8 years and adults</td>
<td>500mg bd</td>
</tr>
</tbody>
</table>

Adapted from the BNF for Children 2012-2013 and HPA Guidelines

Other measures to reduce risk include:

- Patients should be asked to consult if they have a febrile illness and may be given a stock of antibiotics to start treatment by themselves. They should carry a card and/or Medic-Alert bracelet or necklace.
- When travelling abroad patients should obtain advice from a reputable travel advice centre (e.g. Liverpool School of Tropical Medicine) to ensure precautions are adequate and up to date.
- Patients should avoid malaria (which is more severe in asplenic patients) by avoiding malarial areas or, if going to such areas, adhere scrupulously to antimalarial prophylaxis and anti-mosquito precautions.
- Avoid tick bites as there is a risk of Babesiosis and Lyme disease.

The length and timing of commencement of prophylaxis is determined by the regime required. Regular GP literature also provides updated advice on the choice of antimalarials for different regions of the world. Further information is available from the Liverpool School of Tropical Medicine on 0151 708 5933.

Prophylactic medicines do not provide absolute protection against malaria. Personal protection against being bitten using mosquito nets, insect repellents and appropriate clothing is also important.

A leaflet entitled “Malaria. Information for people travelling overseas” is available from www.hpa.org.uk

For further information please see the Malaria Prophylaxis Prescribing Policy at: http://mm.wirral.nhs.uk/document_uploads/policies/PPMalariaProphylaxisv1-1.pdf
PAEDiatric DOSES

Amoxicillin
1 month to 1 year 62.5mg tds
1 to 5 years 125mg tds
5 to 18 years 250mg tds
Doses of 40mg/kg/day in 3 divided doses (max. 1.5g daily) are recommended in the treatment of Acute Otitis Media.
Doses may be doubled in severe infections

Augmentin-Deo
(Preparation for bd dosing)
2 months to 2 years 400/57 suspension
2 to 6 years (13 to 21kg) 0.15mg/kg bd
7 to 12 years (22 to 40kg) 2.5ml bd
Doses may be doubled in severe infection

Azithromycin
Over 6 months 10mg/kg once daily
or
Body weight 15 to 25kg 200mg once daily for 3 days
Body weight 26 to 35kg 300mg once daily for 3 days
Body weight 36 to 45kg 400mg once daily for 3 days
Body weight over 45kg 500mg once daily for 3 days

Cefaclor
1 month to 12 years 12.5mg/kg twice daily.
Dose may be doubled in severe infection
or
1 month to 1 year 125mg bd
1 to 5 years 250mg tds
5 to 12 years 500mg 2 to 3 times daily, increased to
1 to 1.5g 3 to 4 times daily for severe infection

Cefixime
6 months to 1 year 75mg daily
1 to 5 years 100mg daily
5 to 10 years 200mg daily
10 to 18 years 200mg-400mg daily or 100mg - 200mg twice daily

Clarithromycin
1 month to 12 years
Body weight under 8kg 7.5mg/kg bd
Body weight 8 to 11kg 62.5mg bd
Body weight 12 to 19kg 125mg bd
Body weight 20 to 29kg 187.5mg bd
Body weight 30 to 40kg 250mg bd
12 to 18 years 250mg bd for 7 days, increased if necessary in severe infections to 500mg every 12 hours for up to 14 days

Co-Ampicillin
1 month to 1 year 0.25mg/kg tds of 125/31 suspension
1 to 6 years 5ml tds of 125/31 suspension
6 to 12 years 5ml tds of 250/62 suspension
Doses may be doubled in severe infection

Erythromycin
1 month to 2 years 125mg qds
2 to 8 years 250mg qds
8 to 18 years 500mg qds
Doses may be doubled in severe infections
Total daily dose may be given in two divided doses.

Flucloxacillin
1 month to 2 years 62.5 to 125mg qds
2 to 10 years 125 to 250mg qds
10 to 18 years 250 to 500mg qds

Metronidazole
For anaerobic infections
1 month to 12 years 7.5mg/kg (maximum 400mg) every 8 hours
12 to 18 years 400mg every 8 hours

Nitrofurantoin
Contra-indicated under 3 months
3 months to 12 years 750 micrograms/kg qds for 3 to 7 days
12 to 18 years 500mcg qds for 3 to 7 days, increased to 100mg qds in severe chronic recurrent infections

Phenoxymethylpenicillin (Penicillin V)
1 month to 12 years 62.5mg qds
1 to 6 years 125mg qds
6 to 12 years 250mg qds
(Increased in severe infection to ensure at least 12.5mg/kg qds)
12 to 18 years 500mg qds, increased in severe infections up to 1g qds
Give at least 30 minutes before food

Trimethoprim
1 month to 12 years 4mg/kg (maximum 200mg) bd
or
6 weeks to 6 months 25mg bd
6 months to 6 years 50mg bd
6 to 12 years 100mg bd
12 to 18 years 200mg bd
For chronic infections or prophylaxis of urinary tract infection:
1 month to 12 years 2mg/kg (maximum 100mg) once daily at night
12 to 18 years 100mg once daily at night
REFERENCES


25. Faculty of Sexual and Reproductive Healthcare (FSRH), British Association for Sexual Health and HIV (BASHH), Management of vaginal discharge in non-genitourinary medicine settings. London (UK): Faculty of Sexual and Reproductive Healthcare (FSRH); February 2012. http://www.bashh.org/documents/4264


32. NICE Clinical Guideline 102. Bacterial Meningitis and Meningococcal Septicaemia. June 2010


OTHER SOURCES OF INFORMATION

- Standing Medical Advisory Committee Sub-Group on Antimicrobial Resistance “The Path of Least Resistance”. Department of Health 1998. This can be accessed via www.dh.gov.uk

- British National Formulary (BNF), British Medical Journal and Royal Pharmaceutical Society of Great Britain 2012; 64

- Immunisation Against Infectious Disease 2006 - “The Green Book.” This can be accessed via: http://immunisation.dh.gov.uk/category/the-green-book/

- Health Protection Agency - www.hpa.org.uk particularly:
  - HPA and Association of Infection Guidance for Primary Care for Consultation and Local Adaptation. (Last reviewed July 2010). Accessed via www.hpa.org.uk

- Map of Medicine via www.wirral.mapofmedicine.com

- Antibiotic Resistance Campaign - www.dh.gov.uk/en/Publichealth/Patientsafety/Antibioticresistance/DH_082512

- YOUR LOCAL MICROBIOLOGISTS
  Dr John Cunniffe, Dr David Harvey and Dr Kavya Mohandas

HOW TO OBTAIN ANTIBIOTIC RESOURCES

- Contact the Medicines Management Team on 0151 643 5338 or visit the Medicines Management Internet site via - http://mm.wirral.nhs.uk/default.aspx

- Department of Health Website - www.dh.gov.uk/

- Patient UK www.patient.co.uk/DisplayConcepts.asp?f=1&maxresults=&WordId=infection

APPENDIX 1 - Antibiotic Monographs

These monographs are intended as a guide only and should be used alongside the information in the BNF especially for areas such as doses, cautions, contra-indications, interactions and adverse events, which are not covered exhaustively in this section.

Traffic light colours will be used throughout the monograph section to highlight the propensity of an antibiotic to cause Clostridium difficile infection.

RED = High Risk
GREEN = Lower Risk

Aciclovir

Interactions: Probenecid may reduce the excretion of aciclovir (increased plasma concentration).

Acetic acid 2% (EarCalm)

Dosage: One spray into the affected ear tds for a maximum of 7 days.

Dosage: 250 to 500mg tds.

Contra-indications: Penicillin hypersensitivity.

Interactions: May reduce the excretion of methotrexate leading to toxic effects.

Clostridium difficile risk - medium

Cefalexin

Dosage: 500mg daily for 3 days.

Administration: Take 1 hour before food or on an empty stomach.

Contra-indications: Hepatic impairment.

Interactions: Absorption is reduced by antacids. Levels of ciclosporin and digoxin may be increased.

Clostridium difficile risk - medium

Cefalexin

Dosage: 250mg every 6 hours or 500mg every 8 to 12 hours. Maximum dose in moderate to severe renal impairment 500mg every 12 hours.

Side effects: Diarrhoea and rarely antibiotic associated colitis (CSM has warned that both more likely with higher doses).

Clostridium difficile risk - medium-high
Ciprofloxacin

Cautions and Contra-indications: Quinolones should be used with caution in patients with a history of epilepsy and in children or adolescents. Dose reduction is needed in severe renal impairment.

Interactions: See Levofloxacin. Also anticoagulant effect of warfarin enhanced. May increase the plasma concentration of theophylline.

Side effects: CSM has warned that quinolones may induce convulsions in patients with or without a history of convulsions; taking NSAIDs at the same time may also induce them. Tendon rupture can occur within 48 hours of starting treatment; elderly patients and those on concomitant steroids are most at risk. If tendonitis is suspected, the quinolone must be stopped immediately.

Clostridium difficile risk - medium-high (especially in 027 strains)

Dosage: 500mg every 12 hours. Maximum dose in severe renal impairment 250mg every 12 hours.

Cautions and Contra-indications: Avoid concomitant administration with pimozide or terbinafine.

Interactions: May enhance anticoagulant effect of warfarin. Risk of disopyramide toxicity with concomitant use. Increases carbamazepine, phenytoin, ciclosporin and tacrolimus concentrations. May increase levels of simvastatin and atorvastatin.

Side effects: See under erythromycin.

Clostridium difficile risk - medium

Dosage: 375mg every 8 hours, 625mg every 8 hours in severe infections.

Cautions and Contra-indications: Contra-indicated in any patient with a history of co-amoxiclav or penicillin-associated jaundice or hepatic dysfunction. Caution in hepatic disease or impairment.

Interactions: See amoxicillin.

Side effects: CSM has advised that cholestatic jaundice can occur either during or shortly after the use of co-amoxiclav. Cholestatic jaundice is more common in patients above the age of 65 years and in men; these reactions have only rarely been reported in children. The duration of treatment should be appropriate to the indication and should not normally exceed 14 days.

Clostridium difficile risk - medium

Dosage: 200mg on day 1 then 100mg daily thereafter. For severe infections 200mg daily.

Cautions and Contra-indications: Caution in hepatic impairment and with hepatotoxic drugs.

Interactions: Carbamazepine, phenytoin and primidone may increase the metabolism of doxycycline. Doxycycline may enhance the anticoagulant effect of warfarin. Avoid concomitant use with isotretinoin as can cause benign intracranial hypertension.

Side effects: Oesophageal irritation.

Clostridium difficile risk - low to medium

Dosage: 250mg to 500mg every 6 hours or 500mg to 1g every 12 hours. Up to 4g daily in severe infection. Reduce dose in hepatic impairment. Maximum dose in severe renal impairment is 500mg every 8 hours.

Cautions and Contra-indications: Avoid concomitant administration with pimozide or terbinafine.

Interactions: See clarithromycin.

Side effects: Rash, less frequently hepatic disorders and hypersensitivity reactions.

Fluconazole

Dosage: Vaginal candidiasis 150mg as a stat dose.

Side effects: Prolongation of QT interval causing ventricular tachycardia.

Clostridium difficile risk - medium to high (especially in 027 strain)
Dosage: 408mg daily for at least 8 weeks
Cautions and Contra-indications: Should not be given to children under 12 years of age or to pregnant or breast-feeding women as deposition of tetracyclines in growing bones and teeth (by binding to calcium) causes staining and occasionally dental hypoplasia. Avoid in liver and renal disease.

Clostridium difficile risk - low to medium

Mebendazole
Side effects: Very rarely abdominal pain, diarrhoea, convulsions (in infants) and rash.

Metronidazole
Dosage: 400mg tds for Clostridium difficile infection.
Cautions and Contra-indications: Caution in hepatic impairment and hepatic encephalopathy as high plasma concentrations may cause symptoms of encephalopathy.
Interactions: Avoid alcohol during treatment and for at least 48 hours after last dose (risk of disulfiram-like reaction). May enhance anticoagulant effect of warfarin. Plasma concentrations of phenytoin increased. Metabolism of metronidazole increased by primidone. Lithium intoxication has been reported, avoid concurrent administration.
Side effects: Gastrointestinal disturbances, unpleasant taste, darkening of urine and peripheral neuropathy.

Clostridium difficile risk - low

Nitrofurantoin
Contra-indications: Contra-indicated if creatinine clearance <60ml/minute.
Side effects: Urine may be coloured yellow or brown. Acute and chronic pulmonary reactions, peripheral neuropathy and hypersensitivity reactions may occur.

Clostridium difficile risk - low

Ofloxacin
Cautions and Contra-indications: Epilepsy. History of tendon disorders due to quinolone administration, children and growing adolescents. Hepatic impairment and history of psychiatric illness. May affect performance of skilled tasks (e.g. driving). Effects enhanced by alcohol.
Interactions: Absorption reduced by antacids and iron. Separate administration by at least 2 hours.
Side effects: Tendon rupture can occur within 48 hours of starting treatment; elderly patients and those on concomitant steroids are most at risk. If tendonitis is suspected, ofloxacin must be stopped immediately.

CSM has warned that quinolones may induce convulsions in patients with or without a history of convulsions; taking NSAIDs at the same time may also induce them.

Clostridium difficile risk - medium to high (especially in 027 strain)

Phenoxyethylpenicillin (Penicillin V)
Dosage: 500mg every 6 hours, increased to 750mg every 6 hours in severe infections.
Contra-indications: Penicillin hypersensitivity.
Side effects: Hypersensitivity reactions including urticaria.
Administration: Take on an empty stomach or 1 hour before food to enhance absorption.

Clostridium difficile risk - low

Trimethoprim
Dosage: 200mg every 12 hours.
Cautions and Contra-indications: Avoid in patients with blood dyscrasias.
Interactions: May increase phenytoin levels. Increased risk of nephrotoxicity with ciclosporin. Increased risk of haematological toxicity with azathioprine. Increased antifolate effect of metotrexate - avoid concomitant use.
Side effects: Blood disorders on long-term treatment. Patients should be told how to recognise signs of blood disorders and advised to seek medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.

Clostridium difficile risk - low

Key messages for City/Hospital Doctors and Consultants

Patients are referred to Wirral Community Nursing Service by:
• Discharging Hospital Doctor or Consultant (for patients requiring intravenous antibiotics on discharge from hospital to facilitate early discharge).
• or
• Patient’s own GP (for patients requiring initiation of intravenous antibiotics in the community to avoid admission to hospital).

The referrer will retain responsibility for any monitoring and /or review of the patient.

Patient Selection:
• The patient must be over 16 years of age.
• The patient has been assessed as fit for early supported discharge or to prevent hospital admission.
• Confirmation has been given by the medical referrer that they will remain responsible for any re-assessment of the patient's condition.
• There is no available treatment via any other route which could be prescribed as an alternative.
• The patient has not previously suffered an anaphylactic reaction
• The referring doctor has discussed treatment with a consultant microbiologist and there are no contraindications to the proposed treatment.
• The patient has been prescribed an antibiotic that is on the agreed list of medicines in the Standard Operating Procedure for Administration of Intravenous Antibiotics, Wirral Community NHS Trust.
• The patient’s home situation must be suitable. There should be running water and access to a telephone, adequate lighting and sufficient space to maintain a sterile field.

Prescribing
• It is the responsibility of the patient’s own GP to prescribe intravenous antibiotics, diluents and flushes on a FP10 prescription.
• The referrer must contact the Microbiologist for advice on the correct antibiotic and route of administration. The Patient Medicines Administration Chart (PMAC) must be endorsed with "Discussed with the Microbiologist".
• The GP must complete and sign a Patient Medicines Administration Chart (PMAC)
• The prescriber must provide clear, precise written instructions regarding the medicine, dose, frequency of administration and duration of treatment as well as allergy status. Verbal orders for commencement of or changes to intravenous medications will NOT be taken.

Supplies of Intravenous Antibiotics:
• The antibiotics plus diluents and flushes must be prescribed on a FP10 prescription. The FP10 prescription must be filled by a Community Pharmacy. Ringing the Community Pharmacy in advance is good practice in order to allow them to order in stock where necessary.
• If the prescribed antibiotics are not immediately available commencement of treatment will have to be delayed until a supply is available. Wirral Community Nursing Service do not stock drugs.
• Lloyds Pharmacy, Arrowe Park Hospital site keep a selected list of IV antibiotics (plus diluents / flushes) in stock for the Wirral Community Nursing Service Team.
APPENDIX 3
Sharing Good Practice

Useful tips from GPs and nurses at an antibiotic educational event (February 2009)

Obstacles to Rational Antibiotic Prescribing

• Patient expectations and demands.
• Perceived employers’ expectations.
• Time pressures.
• Language challenges.
• Care Home demands.
• Incorrect or incomplete documentation of drug allergies.
• Pressure from childcare establishments.
• Lack of consistency between partners in a practice.

Potential Solutions

• Educate patients via:
  • Local radio adverts.
  • Mail shots.
  • Explanation of the duration of anticipated symptoms.
  • Advising patients to visit their local pharmacy first for advice and symptomatic treatment.
  • Promoting messages to the media - how about antibiotic stories in soap operas?
  • Use of the language line if language barriers experienced.

• Do not “give in” to patient demand and consider that the patient might not actually want an antibiotic - just reassurance.
• Use of delayed antibiotic prescriptions.
• Use microbiology tests where appropriate before prescribing an antibiotic.
• Educate employers / Care Homes / Childcare establishments.
• Regular review of guidelines.
• Meeting with all GPs and practice pharmacist. Open discussion in practices about individual GP prescribing habits.
• Prescribers must be consistent in their messages and prescribing.
• Ensure all locums obtain educational messages, including the antibiotic guidelines.
• More antibiotic resources available to more centres!
• Audit and evaluation.
• Use microbiology services and infection control.

APPENDIX 4
Members of the Antibiotic Guideline Working Group

Dr J G Cunniffe  Medical Microbiologist, Wirral University Teaching Hospital NHS Foundation Trust (Medical Lead)
Dr R Gokhale  Clinical Lead and Consultant in GU Medicine and HIV, Wirral University Teaching Hospital NHS Foundation Trust
Dr Y Graham  Consultant, Sexual Health Services, NHS Wirral
Dr A Lee  GP Prescribing Lead, WGPCC
Mrs H Oulton  Lead Nurse/Manager Infection Prevention & Control, Wirral Community Trust
Dr B Taylor  Medicines Management Lead, WHCC
Mrs N Bradley  Practice Pharmacist, NHS Wirral (Medicines Management Lead)
Dr H Downs  GP Prescribing Lead, Wirral NHS Alliance

Contact details for further information

Medical Lead
Dr J Cunniffe 0151 604 7601 or 0151 604 7607
Medicines Management Lead 0151 643 5319
Guidelines for the empiric use of antimicrobials in adults

HSE South East Hospitals:

Waterford Regional Hospital
South Tipperary General Hospital
Kilcreene Orthopaedic Hospital
St. Luke’s General Hospital, Kilkenny
Wexford General Hospital

June 2013

Review Date: June 2014
Acknowledgement: Gentamicin and Vancomycin Algorithms page 23 & 25 adapted from original algorithms kindly provided by Beaumont/Connolly Hospital Antimicrobial Stewardship Committee in 2011.

Issued in June 2006
Revised Annually
Revision No 7
Review Date June 2014

HSE SE Antimicrobial Stewardship Group

Disclaimer:
Whilst every effort has been made to ensure the accuracy of the information and material contained in this document, errors or omissions may occur in the content. We acknowledge that new evidence may emerge that may overtake some of these recommendations. The document will be reviewed and revised as and when appropriate. Prescribers should ensure that the correct drug and dose is prescribed, as is appropriate for each individual patient. References that should be used in conjunction with these guidelines include the British National Formulary (BNF) and the drug data sheets (available on www.medicines.ie). Clinical guidelines are guidelines only and the interpretation and application of the guidelines remains the responsibility of the individual clinician.

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Guidance</td>
<td>2 - 3</td>
</tr>
<tr>
<td>Restricted and Reserve Antimicrobials</td>
<td>4</td>
</tr>
<tr>
<td>MRSA</td>
<td>5</td>
</tr>
<tr>
<td>Septicaemia/Systemic Sepsis</td>
<td>6 - 7</td>
</tr>
<tr>
<td>Sepsis in Pregnancy, Neutropenic Sepsis</td>
<td></td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>8</td>
</tr>
<tr>
<td>Respiratory Tract Infection</td>
<td>9 - 14</td>
</tr>
<tr>
<td>Endocarditis &amp; Intra-abdominal Infections</td>
<td>14</td>
</tr>
<tr>
<td>Gastro-intestinal Infection</td>
<td>15</td>
</tr>
<tr>
<td>Start Smart Then Focus Care Bundle</td>
<td>16 - 17</td>
</tr>
<tr>
<td>Genital Tract Infection</td>
<td>18</td>
</tr>
<tr>
<td>Bone and Joint Infections</td>
<td>19</td>
</tr>
<tr>
<td>Skin and Soft tissue Infections</td>
<td>19</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>20</td>
</tr>
<tr>
<td>ENT infections</td>
<td>20</td>
</tr>
<tr>
<td>Appendix 1: Start Smart, Then Focus Care Bundle</td>
<td>21</td>
</tr>
<tr>
<td>Appendix 2: Gentamicin</td>
<td>22 - 23</td>
</tr>
<tr>
<td>Appendix 3: Glycopeptides: Vancomycin, Teicoplanin</td>
<td>24 - 25</td>
</tr>
<tr>
<td>Appendix 4: Treatment of Clostridium difficile Infection</td>
<td>26 - 27</td>
</tr>
<tr>
<td>Appendix 5: Switch from IV to PO</td>
<td>28 - 29</td>
</tr>
<tr>
<td>Appendix 6: Contingency Plan in Eventuality of Shortage of Intravenous Co-amoxiclav</td>
<td>30</td>
</tr>
<tr>
<td>Appendix 7: Relative Costs of Antimicrobials</td>
<td>31</td>
</tr>
<tr>
<td>References</td>
<td>32</td>
</tr>
</tbody>
</table>
**GENERAL GUIDANCE**

1. **NB:** The prescriber should always check prescribing information such as cautions, contraindications, interactions and side effects when considering antimicrobial therapy. Ensure information on antimicrobial prescribing, including risks and side effects associated with antimicrobial treatment, is available to patients or their legal guardians.¹

2. Where possible indicate intended duration of therapy at point of initial prescribing. Review IV antimicrobial therapy daily.

3. Document indication for therapy and intended duration in medical record. Note these guidelines are intended for **empiric therapy.** Rationalise when microbiology results become available. **It is the responsibility of the person/team ordering laboratory tests to follow up on the results to guide appropriate clinical management of the patient.**

4. Piperacillin-tazobactam and co-amoxiclav provide **good anaerobic cover.** Concurrent metronidazole is **NOT** required unless there is gross faecal contamination — e.g. faecal peritonitis. Treatment of aspiration pneumonia does **NOT** require addition of metronidazole to either of these antibiotics.

5. Some antibiotics e.g. **ciprofloxacin, levofloxacin, fusidic acid and metronidazole** have **excellent oral bioavailability** and the oral route should be used where possible. IV formulations of these should **only** be used if the patient is **not absorbing or unable to have oral medications.**
6. Oral switch – consider when patient is afebrile and infection parameters are settling for 48 hours and normal oral absorption. Generally NOT appropriate in meningitis, endocarditis, febrile neutropenia or acute osteomyelitis/septic arthritis.

7. For oral switch guidelines see pg 28. Oral switch is usually to PO formulation of same antibiotic where available, except IV penicillin to PO amoxicillin as oral absorption of penicillin is very poor.

8. **Penicillin allergy: obtain & document proper history.** If IgE mediated allergic reaction (e.g. anaphylaxis, angioneurotic oedema, immediate urticaria) avoid all beta-lactams. If rash only, a cephalosporin may be considered. Erythromycin is often NOT a good substitute.

9. Flucloxacillin and other betalactams such as co-amoxiclav, piperacillin-tazobactam, cephalosporins and meropenem **do not cover MRSA.**

10. Risk of *Clostridium difficile* associated with all antibiotic use. Particular risk with all fluoroquinolones (e.g. levofloxacin and ciprofloxacin), clindamycin and cephalosporins.
**Restricted/Reserve Antimicrobials:**

A Cochrane review has found that reserving access to selected antimicrobials is the most effective component of any Antimicrobial Stewardship Programme.\(^\text{10}\)

Below is the list of Restricted and Reserve antimicrobials for the SE Acute Hospitals. These antimicrobials should only be prescribed when this is in line with the recommendations of this guideline or following discussion with the Clinical Microbiologist.

Indication for therapy and any discussions/advice from the Clinical Microbiologist should be documented accurately in patient’s medical record.

Restrictions are in place which limit access to these Antimicrobials. Please refer to *South East Acute Hospitals Guidelines for use of Reserve and Restricted Antimicrobials* for details.

<table>
<thead>
<tr>
<th><strong>Restricted Antimicrobials</strong></th>
<th><strong>Reserve Antimicrobials</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Piperacillin/Tazobactam</td>
<td>IV Cefotaxime</td>
</tr>
<tr>
<td>IV Ceftriaxone</td>
<td>IV Ceftazidime</td>
</tr>
<tr>
<td>IV Ciprofloxacin</td>
<td>IV Erythromycin</td>
</tr>
<tr>
<td>IV/PO Levofloxacin</td>
<td>IV Ofloxacin</td>
</tr>
<tr>
<td>IV Chloramphenicol</td>
<td>IV Colistin</td>
</tr>
<tr>
<td>IV/PO Clindamycin</td>
<td>IV Daptomycin</td>
</tr>
<tr>
<td>IV Teicoplanin</td>
<td>IV Tigecycline</td>
</tr>
<tr>
<td>IV Vancomycin</td>
<td>PO Fidaxomicin</td>
</tr>
<tr>
<td>IV/PO Linezolid</td>
<td>IV Ceftaroline</td>
</tr>
<tr>
<td>IV Meropenem</td>
<td>IV/PO Fosfomycin</td>
</tr>
</tbody>
</table>

**Antifungals**

- Liposomal Amphotericin B
- Anidulafungin
- Caspofungin
- Voriconazole
- Posaconazole

*Reserve antimicrobials should only be prescribed when recommended by a Consultant and following discussion with the Clinical Microbiologist.*
**MRSA**  
*(Meticillin Resistant Staphylococcus aureus)*

**Infection with MRSA should be suspected if:**

- Patient has previously been colonized with MRSA. (Please check patients notes or check laboratory enquiry for ‘SIF code’)
- Recent hospitalization (within 12 months)
- Transfer from another hospital or long term care facility.
- Other situation where increased clinical suspicion of MRSA (Please refer to most recent edition of: Policy on Control and Prevention of Meticillin Resistant Staphylococcus aureus (MRSA) in Acute Hospitals in the HSE/SE for additional information)

**If MRSA infection is suspected, consider including a glycopeptide** (Vancomycin or Teicoplanin, see page 24) in the empiric treatment regimen.

**MRSA eradication:** Please refer to most recent edition of: Policy on Control and Prevention of Meticillin Resistant Staphylococcus aureus (MRSA) in Acute Hospitals in the HSE/SE.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septicaemia/ Systemic Sepsis</td>
<td>Initial empirical therapy if no obvious source: Piperacillin-tazobactam 4.5g IV TDS. Consider adding gentamicin if haemodynamically unstable / severe infection. Consider need for additional gram positive cover e.g vancomycin (or teicoplanin if patient is already on gentamicin)</td>
<td>Consider if patient at risk for infection due to MRSA, if so, add vancomycin. Consider other multiresistant organisms eg ESBL, VRE, CRE. Watch for hypotension</td>
</tr>
<tr>
<td></td>
<td>Penicillin allergy: Gentamicin, metronidazole plus teicoplanin</td>
<td>Check previous laboratory results. Ensure blood cultures taken. See individual infection treatment guidelines for appropriate therapy. Refer to NEWS Score of the adult patient observation chart and Sepsis Six.</td>
</tr>
</tbody>
</table>

### CONSIDER SEPSIS

Sepsis = Known or Suspected Infection & Systemic Inflammatory Response Syndrome (SIrS)

- Defined as the presence of 2 or more of the following:
  - Temperature $> 38^\circ\text{C}$ or $< 36^\circ\text{C}$
  - Respiratory Rate $> 20$ breath per min
  - $\text{PaCO}_2 < 4.3$ kPa
  - Heart Rate $> 90$ beats per min
  - White Cell Count $> 12$ or $< 4$

### Intervention:
- Action within One Hour
  - COMPLETE SEPSIS SIX
- 1. High Flow Oxygen
- 2. Lactate Check
- 3. Fluid Challenge
- 4. Urine Monitoring
- 5. Cultures*
- 6. Antimicrobial Therapy

* blood, wounds, invasive line sites, sputum, urine etc as appropriate

Adapted from: HSE Adult Patient Observation Chart

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Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenic sepsis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Neutropenia = Neutrophil Count &lt; 1.0&lt;br&gt;Severe Neutropenia = Neutrophil Count &lt; 0.5&lt;br&gt;Fever = Temperature &gt; 38°C</td>
<td>Initial Empiric therapy: Piperacillin-tazobactam 4.5g QDS IV. Add gentamicin if complications (e.g. hypotension, pneumonia or antimicrobial resistance suspected or critically ill). Consider adding vancomycin or teicoplanin for specific clinical indications e.g. suspected CVC-related infection or complications as above. Penicillin allergy (Not Severe reaction anaphylaxis): Ceftazidime 2g TDS IV plus vancomycin or teicoplanin. Severe reaction/anaphylaxis to penicillin: Ciprofloxacin plus gentamicin plus teicoplanin</td>
</tr>
<tr>
<td>Sepsis in Pregnancy</td>
<td>Refer to Septicaemia/ Systemic Sepsis on p6. Clinical features suggestive of sepsis in pregnant women: Fever/Rigors, Diarrhoea/ Vomiting, Rash, Abdominal/ Pelvic Pain and Tenderness, Offensive Vaginal Discharge, Cough, Urinary Symptoms&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Initial empirical therapy: Piperacillin-tazobactam 4.5g IV TDS. Consider adding gentamicin if haemodynamically unstable / severe infection. Consider need for additional gram positive cover e.g vancomycin (or teicoplanin if patient is already on gentamicin) Add clindamycin if invasive group A Strep Infection suspected.</td>
</tr>
<tr>
<td>Condition</td>
<td>Antibiotic</td>
<td>Comments</td>
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<tr>
<td>------------------------------------------</td>
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</tr>
<tr>
<td>Lower urinary tract infection (uncomplicated)</td>
<td>First line: Nitrofurantoin MR 100mg BD PO for 5 days</td>
<td>Nitrofurantoin is not appropriate if creatinine clearance is &lt; 50 ml/min, use co-amoxiclav (If not allergic to penicillin (discuss if needed)) In pregnancy nitrofurantoin may also be used but it should be avoided at term.</td>
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<tr>
<td></td>
<td>Second line: Co-Amoxiclav 625mg TDS PO for 3 days</td>
<td>Patients with recurrent UTIs may have resistant organisms. Use 7-10 days treatment in males.</td>
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<tr>
<td></td>
<td>(In penicillin allergy discuss with Microbiologist)</td>
<td></td>
</tr>
<tr>
<td>Hospital acquired or recurrent UTI or complicated UTI</td>
<td>Refer to recent culture results. If septicaemic: as for pyelonephritis</td>
<td></td>
</tr>
<tr>
<td>Catheter associated UTI</td>
<td>For patients with catheter associated UTIs, antibiotics are unlikely to resolve the UTI unless the catheter is removed. If systemic sepsis suspected treat as per Pyelonephritis.</td>
<td></td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>Piperacillin-tazobactam 4.5g TDS for 10-14 days or gentamicin (see page 18 for dosing regimen).</td>
<td>Send blood cultures and MSU. Rationalise therapy as soon as possible. Check culture and antimicrobial sensitivity results.</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>Ciprofloxacin 500-750mg BD PO for 2-6 weeks.</td>
<td>Relapse common. Follow up advised. Check antimicrobial sensitivity where possible.</td>
</tr>
</tbody>
</table>
COMMUNITY ACQUIRED PNEUMONIA

These guidelines are not aimed at:
(a) Patients with known predisposing conditions such as cancer or immunosuppression admitted with pneumonia to specialist units such as oncology, haematology, palliative care, infectious disease units or AIDS units
(b) Adults with non pneumonic LRTI, including illnesses labelled as acute bronchitis, acute exacerbations of COPD or “chest infections”

<table>
<thead>
<tr>
<th>Respiratory Tract Infections</th>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
</table>
|                              | Community Acquired Pneumonia               |            | Community Acquired Pneumonia:
Assess severity using CURB-65 score as per BTS guidelines:
Confusion (new onset)
Urea >7mmol/L
RR≥30/min
BP - hypotensive: SBP <90mmHg or DBP ≤60mmHg
Age ≥ 65 years
CURB-65 score should be used with caution in younger patients as it may underestimate severity in these patients. |
<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Community Acquired Pneumonia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low severity (CURB65 = 0-1)</td>
<td>Amoxicillin 500mg tds PO. (IV if PO administration not possible.) Penicillin allergy: clarithromycin 500mg BD or doxycycline 200mg OD PO loading dose then 100mg OD PO.</td>
<td>No microbiological tests required. 7 days appropriate antibiotic therapy is recommended.</td>
</tr>
<tr>
<td>Moderate Severity (CURB65 = 2)</td>
<td>Amoxicillin 500mg-1.0g tds PO plus clarithromycin 500mg bd PO. (IV if PO administration not possible.) Penicillin allergy: PO doxycycline</td>
<td>Microbiology: Send blood cultures, sputum, urine for pneumococcal antigen. 7 days appropriate antibiotic therapy is recommended.</td>
</tr>
<tr>
<td>High severity (CURB65 = 3-5)</td>
<td>Co-amoxiclav 1.2g tds IV plus clarithromycin 500mg bd IV. (If legionella strongly suspected consider adding levofloxacin) Penicillin allergy (NOT IgE mediated reaction/anaphylaxis): cefuroxime 750mg-1.5g tds IV plus clarithromycin 500mg bd IV. Severe IgE mediated reaction/anaphylaxis to penicillin: levofloxacin 500mg PO/IV OD (12 hourly if severe).</td>
<td>Microbiology: Send blood cultures, sputum (requesting legionella culture), urine for pneumococcal antigen and legionella antigen, CRP. Consider switch to PO antibiotics as soon as clinical improvement occurs and patient is apyrexial for 24 hours. 7-10 days appropriate antibiotics is proposed. This may need to be extended to 14-21 days according to clinical judgement.</td>
</tr>
<tr>
<td>Legionellosis</td>
<td>Levofloxacin 500mg PO/IV OD (12 hourly if severe) Discuss with Microbiologist.</td>
<td>IV route to be used if oral absorption unreliable. Early oral switch where possible.</td>
</tr>
</tbody>
</table>

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013 Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
BTS-recommended therapy for Community Acquired Pneumonia
(Taken from J Antimicrob Chemother 2012; 65: page 612) 

**CURB65 score**
- New onset mental confusion
- Urea > 7 mmol/L
- Respiratory rate ≥ 30/min
- Systolic blood pressure < 90 mmHg and/or
diastolic blood pressure ≤ 60 mmHg
- Age ≥ 65 years

**Low risk**
- 0 or 1 point
- Outpatient management
- Oral amoxicillin

**Intermediate risk**
- 2 points
- Inpatient management
- Oral amoxicillin
- and macrolide

**High risk**
- 3-5 points
- Inpatient management
- Intravenous co-amoxiclav
- and macrolide

CURB-65 score should be used with caution in younger patients as it may underestimate severity in these patients

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health care associated pneumonia ¹</td>
<td>Patients from nursing home/chronic care nursing facility/recent hospitalisation refer to algorithm page 13.</td>
<td></td>
</tr>
<tr>
<td>Hospital acquired pneumonia ¹</td>
<td>Co-amoxiclav 625mg TDS PO or 1.2g TDS IV for 8 days. Penicillin allergy (NOT IgE mediated reaction /anaphylaxis): Cefuroxime 750 mg -1.5g TDS IV. Severe IgE mediated reaction/anaphylaxis to penicillin: Levofloxacin 500mg PO / IV OD. (12 hourly if severe). Piperacillin-tazobactam 4.5g TDS IV If risk factors for MDR pathogens see page 13. Penicillin allergy: if NOT IgE mediated/anaphylaxis and if pneumonia is not severe consider cefuroxime 1.5g TDS IV. Severe IgE mediated reaction/anaphylaxis to penicillin: Levofloxacin 500mg PO/IV OD (12 hourly if severe).</td>
<td>Send sputum for culture if possible. Consider legionella risk. In at risk patients send urine for legionella antigen and add clarithromycin empirically. Send sputum for Legionella culture, if possible. For confirmed legionellosis see page 12. If patient is considered to be high risk for MRSA, consider adding Vancomycin</td>
</tr>
</tbody>
</table>

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
Algorithm for healthcare-associated pneumonia (HCAP) therapy*

**HCAP present:** Patient from nursing home/chronic care facility, recent hospitalization

Assess **severity of illness** (Use CURB65 score)

AND

Presence of risk factors for multi-drug resistant (MDR) pathogens
(antibiotics in past 6 months, hospitalization in past 3 months, poor functional status, immune suppression)

**Severe pneumonia** (Based on CURB65 score)

- **No** (CURB65 score mild or moderate)
  - 0-1 Risks for MDR
  - Treat for common CAP Pathogens
  - See CAP p.8

- **Yes** (CURB65 score 3 or >)
  - ≥2 Risks for MDR
  - Treat for MDR Pathogens
  - See HAP p.10
  - 0 Risks for MDR
  - Treat as severe CAP
  - See CAP p.8
  - ≥1 Risk for MDR
  - Treat for MDR Pathogens
  - See HAP p.10

Patients with HCAP should be identified and then divided on the basis of severity of illness to guide initial therapy. Patients in each group are then further divided based on whether they have risk factors for drug-resistant (MDR) pathogens that include: recent antibiotic therapy in the past 6 months, recent hospitalization in the past 3 months, the presence of immune suppression, and poor functional status as defined by activities of daily living. CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia.

*Adapted from Brito V, et al. Current Opinion in Infectious Diseases 2009, 22:316-325

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Tract Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute exacerbation of COPD</td>
<td>Antibiotics may not be required See “Comments”</td>
<td>Consider antibiotic therapy if 2 or more present:</td>
</tr>
<tr>
<td>(no consolidation on CXR)</td>
<td>Co-amoxiclav oral or IV depending on severity for 5-7 days. Review need for IV therapy on a daily basis.</td>
<td>Increased breathlessness</td>
</tr>
<tr>
<td></td>
<td>Penicillin allergy : Clarithromycin 500mg BD daily PO for 5-7 days</td>
<td>Increased sputum volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sputum purulence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If consolidation on CXR treat as CAP.</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>Seek advice from Microbiology.</td>
<td>Send 3 sets of blood cultures.</td>
</tr>
<tr>
<td>Intra-abdominal infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Examples: Peritonitis, Diverticulitis, Biliary tract infections</td>
<td>Co-amoxiclav 1.2g TDS IV for 7-10 days.</td>
<td>Penicillin allergy (NOT IgE mediated reaction/anaphylaxis):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>First line: Co-amoxiclav 1.2g TDS IV</td>
<td>Severe hypersensitivity reaction/anaphylaxis to penicillins:</td>
</tr>
<tr>
<td></td>
<td>Second line: Piperacillin-tazobactam 4.5g TDS IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>metronidazole + gentamicin</td>
</tr>
<tr>
<td>Severe acute necrotising Pancreatitis</td>
<td>First line: Piperacillin-tazobactam 4.5g TDS IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Second line: Meropenem 1g TDS IV. Consider addition of gentamicin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal Infections</td>
<td>Acute gastroenteritis</td>
<td>Antibiotic Treatment most often not necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider antibiotics ONLY if immunosuppressed or signs of systemic sepsis.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discuss with microbiology team.</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>Refer to Appendix 4 at back of booklet.</td>
<td>Discontinue other antibiotics if possible.</td>
</tr>
<tr>
<td>Associated Disease (CDAD)</td>
<td></td>
<td>Discuss with microbiology team if not responding to therapy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refer to HSE SE Clostridium difficile guidelines in the Infection Control Manual available on all wards.</td>
</tr>
</tbody>
</table>
Start Smart, Then Focus
An Antibiotic Care Bundle for Hospitals

Day 1: Start Smart...

1. Start antibiotics **only** if there is clinical evidence of bacterial infection
   - If there is evidence of bacterial infection, prescribe in accordance with your local antibiotic guidelines and appropriately for the individual patient (see notes below)

2. Obtain appropriate cultures before starting antibiotics

3. Document in both the drug chart and medical notes:
   - Treatment indication
   - Drug name, dose, frequency and route
   - Treatment duration (or review date)

4. Ensure antibiotics are given within four hours of prescription
   - Within 1 hour for severe sepsis or neutropenic sepsis

When deciding on the most appropriate antibiotic(s) to prescribe, consider the following factors:
- History of drug allergy (document allergy type: minor (rash only) or major (anaphylaxis, angioedema))
- Recent culture results (e.g. is patient colonised with a multiple-resistant bacteria?)
- Recent antibiotic treatment
- Potential drug interactions
- Potential adverse effects (e.g. *C. difficile* infection is more likely with broad spectrum antibiotics)
- Some antibiotics are considered unsafe in pregnancy or young children
- Dose adjustment may be required for renal or hepatic failure

Consider removal of any foreign body/indwelling device, drainage of pus, or other surgical intervention

For advice on appropriate investigation and management of infections, consult your local infection specialist(s) (microbiologist, infectious disease physician and/or antimicrobial pharmacist)
...then Focus (Day 2 onwards)

At 24-48 hours after starting antibiotics, make an Antimicrobial Prescribing Decision
- Review the clinical diagnosis
- Review laboratory/radiology results
- Choose one of the five options below
- Document this decision

Options
1. Stop antibiotic(s)
   - no evidence of bacterial infection, or infection resolved
2. Switch from intravenous to oral antibiotic(s)
   - if patient meets criteria for oral switch
3. Change antibiotic(s)
   - narrower spectrum, if possible; broader spectrum, if indicated
4. Continue current antibiotic(s)
   - review again after further 24 hours
5. Outpatient parenteral antibiotic therapy
   - consult with local OPAT team

Developed by the RCPI Hospital Antimicrobial Stewardship Working Group (2012)
Adapted, with permission, from the UK Department of Health "Start Smart, Then Focus" hospital antimicrobial stewardship programme
<table>
<thead>
<tr>
<th>Genital Tract Infection</th>
<th>Condition</th>
<th>Antibiotic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic Inflammatory Disease (PID), Salpingitis, Tubo-ovarian abscess</td>
<td><strong>Outpatient Rx:</strong> Ceftriaxone 250mg IM or IV as single dose, then doxycycline PO 100 mg BD + metronidazole PO 400mg TDS</td>
<td><strong>Total duration of therapy:</strong> 14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Inpatient Rx:</strong> Ceftriaxone 1g once daily IV + doxycycline 100mg BD PO + metronidazole PO 400mg TDS</td>
<td><strong>Switch to oral/outpatient regime when satisfactory response for ≥ 24 hours.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Severe IgE mediated reaction/ anaphylaxis to penicillin:</strong> Clindamycin 900 mg IV TDS + gentamicin (refer pg 23) + doxycycline PO 100 mg BD</td>
<td><strong>Note:</strong> Fluoroquinolones (eg ciprofloxacin or ofloxacin) not recommended due to increasing resistance. Ref: MMWR 59 (RR-12)2010 &amp; <a href="http://www.cdc.gov/std/treatment">www.cdc.gov/std/treatment</a></td>
<td></td>
</tr>
<tr>
<td>In pregnancy, a macrolide (azithromycin or erythromycin) may be used instead of doxycycline.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider treating partner.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone and Joint Infections</td>
<td>Condition</td>
<td>Antibiotic</td>
<td>Comments</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
<td>------------</td>
<td>----------</td>
</tr>
<tr>
<td>Osteomyelitis / Septic arthritis</td>
<td>Flucloxacillin 2g QDS IV plus sodium fusidate 500mg tabs TDS PO (or fusidic acid susp. 750mg TDS PO)</td>
<td></td>
<td>Adjust treatment when cultures available. Treat for 4 to 6 weeks. <strong>Monitor CRP.</strong></td>
</tr>
<tr>
<td>Penicillin allergy (NOT IgE mediated reaction/anaphylaxis): Cefuroxime 1.5g TDS IV plus fusidic acid as above.</td>
<td></td>
<td>MRSA known or high risk: vancomycin.</td>
<td></td>
</tr>
<tr>
<td>Severe IgE mediated reaction/anaphylaxis to penicillin: Vancomycin plus fusidic acid as above.</td>
<td></td>
<td>Discuss possible oral switch options with the clinical microbiology team.</td>
<td></td>
</tr>
<tr>
<td>Skin and soft tissue Infections</td>
<td>Cellulitis, erysipelas</td>
<td>Benzylpenicillin (penicillin G) 1.2g-2.4g QDS IV plus flucloxacillin 1-2g QDS IV</td>
<td>Switch to flucloxacillin 500mg-1g QDS PO when clinical improvement achieved. Treat for 10 days minimum. <strong>NOTE:</strong> severe cellulitis should not be treated with a macrolide (erythromycin/clarithromycin). If MRSA suspected use vancomycin.</td>
</tr>
<tr>
<td>Penicillin allergy (NOT IgE mediated reaction/anaphylaxis): Cefuroxime 750mg-1.5g TDS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe IgE mediated reaction/anaphylaxis to penicillin: Clindamycin 1.2g QDS IV.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspected Severe/Invasive Group A Strep Infection</td>
<td>Treat as Necrotising fascitis, see below</td>
<td></td>
<td>If Group A Strep Infection confirmed, consider de-escalation to IV benzylpenicillin plus clindamycin, following discussion with Microbiologist.</td>
</tr>
<tr>
<td>Necrotising soft tissue infections/Necrotising fascitis</td>
<td>Refer to surgical team urgently. Piperaclillin-tazobactam 4.5g IV 6 to 8 hourly plus clindamycin 600mg-1.2g QDS +/- gentamicin.</td>
<td>Modify treatment according to Microbiology results and clinical response.</td>
<td></td>
</tr>
<tr>
<td>Human and animal bites</td>
<td>Co-amoxiclav 625mg TDS (or 1.2g TDS IV if severe) for 5 days</td>
<td></td>
<td><strong>Penicillin allergy:</strong> Doxycycline 100mg BD PO. If severe discuss with microbiology team.</td>
</tr>
<tr>
<td>Condition</td>
<td>Antibiotic</td>
<td>Comments</td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Central Nervous System</td>
<td><strong>Meningitis</strong></td>
<td>**Ceftriaxone 2g BD IV If <em>Listeria</em> risk add amoxicillin 2g 4 hrly IV. If <em>Strep pneumoniae</em> (pneumococcus) or severe infection suspected add vancomycin until sensitivities confirmed. Treat for 14 days if pneumococcus. Treat for 7 days if meningococcus. Severe IgE mediated reaction/anaphylaxis to <em>penicillin</em>: chloramphenicol 1g IV QDS. If immunocompromised add vancomycin and co-trimoxazole. Seek Microbiology advice. Consider Dexamethasone phosphate for bacterial meningitis. (10mg IV 6 hourly for 2 to 4 days. Must commence before or at same time as antibiotic). Send Blood cultures, throat swab, EDTA blood for PCR +/- CSF. Isolate patient. Notify Public Health.</td>
<td></td>
</tr>
<tr>
<td>Encephalitis</td>
<td><strong>Acyclovir 10 mg / kg IV every 8 hours</strong> (use ideal body weight in obese patients)</td>
<td>Adjust dose in renal impairment. Request HSV PCR on CSF.</td>
<td></td>
</tr>
<tr>
<td>ENT Infections</td>
<td><strong>Acute epiglottitis</strong></td>
<td><strong>Ceftriaxone 2g BD IV for 7-10 days</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Tonsillitis/pharyngitis</strong></td>
<td><strong>Phenoxyxymethylpenicillin (penicillin V) 666mg QDS PO for 10 days</strong> Severe: Benzylpenicillin (penicillin G) 1.2g QDS IV <strong>Penicillin allergy</strong>: Consider clindamycin + ciprofloxacin for 7-10 days. <strong>Penicillin allergy</strong>: Clarithromycin 500mg BD PO for 10 days Send throat swab</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Sinusitis, otitis media</strong></td>
<td><strong>Co-amoxiclav 1.2 g IV / 625mg TDS PO for 5-7 days</strong></td>
<td></td>
</tr>
</tbody>
</table>

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
Appendix 1: Start Smart, Then Focus Care Bundle.

Start Smart, Then Focus
An Antibiotic Care Bundle for Hospitals

Day 1: Start Smart...

1. Start antibiotics only if there is clinical evidence of bacterial infection
   - If there is evidence of bacterial infection, prescribe in accordance with your local antibiotic guidelines and appropriately for the individual patient (see notes below)

2. Obtain appropriate cultures before starting antibiotics

3. Document in both the drug chart and medical notes:
   - Treatment indication
   - Drug name, dose, frequency and route
   - Treatment duration (or review date)

4. Ensure antibiotics are given within four hours of prescription
   - Within 1 hour for severe sepsis or neutropenic sepsis

When deciding on the most appropriate antibiotic(s) to prescribe, consider the following factors:
- History of drug allergy (document allergy type: minor (rash only) or major (anaphylaxis, angioedema))
- Recent culture results (e.g. is patient colonised with a multiple-resistant bacteria?)
- Recent antibiotic treatment
- Potential drug interactions
- Potential adverse effects (e.g. C. difficile infection is more likely with broad spectrum antibiotics)
- Some antibiotics are considered unsafe in pregnancy or young children
- Dose adjustment may be required for renal or hepatic failure

Consider removal of any foreign body/indwelling device, drainage of pus, or other surgical intervention

For advice on appropriate investigation and management of infections, consult your local infection specialist(s) (microbiologist, infectious disease physician and/or antimicrobial pharmacist)

...then Focus (Day 2 onwards)

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2. Switch from intravenous to oral antibiotic(s)
   - if patient meets criteria for oral switch
3. Change antibiotic(s)
   - narrower spectrum, if possible; broader spectrum, if indicated
4. Continue current antibiotic(s)
   - review again after further 24 hours
5. Outpatient parenteral antibiotic therapy
   - consult with local OPAT team

Developed by the RCSI Hospital Antimicrobial Stewardship Working Group (2012)
Adapted, with permission, from the UK Department of Health “Start Smart. Then Focus” hospital antimicrobial stewardship programme
Appendix 2: Once daily Aminoglycoside protocol:  
Gentamicin 5mg/kg IV daily
Infuse in 100ml of glucose 5% or sodium chloride 0.9% over 30-60 minutes.

<table>
<thead>
<tr>
<th>Dose Adjustment</th>
<th>Levels</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Suitable for normal renal function, creatinine clearance >80ml/min. Dose reduction if <80ml/min, seek advice. | Pre-dose levels are required to monitor for toxicity  
Clotted sample 16-18h after the first dose of gentamicin should be < 1µg/ml.  
If >1µg/ml: Check timing of level, review dosing schedule, check renal function, consider alternative therapy and seek advice if necessary.  
See page 23 for dosing algorithm.  
If continuing gentamicin and renal function is stable, repeat level twice weekly. Daily levels may be required if renal function is unstable.  
Note: 1-hour post dose levels are not necessary except in endocarditis – please discuss on an individual basis (see comments).  
***Clearly state dose, time of dose and time of blood sample collection on the request form. *** | Endocarditis: 1mg/kg IV 12 hourly.  
Serum levels:  
pre-dose level <1µg/ml  
1 hour post dose level of 3-5µg/ml  
(not always necessary).  
Normal renal function: twice-weekly serum monitoring may be sufficient.  
Abnormal renal function: dosage should be adjusted according to creatinine clearance and daily serum assay results.  
Take pre-dose level before the 3rd dose. |
| NB: Gentamicin doses in excess of 400mg IV / day are rarely required.  
Dose should never exceed 500mg IV/Day.  
See page 23 for dosing algorithm. |                                                                      |                                                                         |

NB Antibiotic assays are done at 12:00 Noon and 4.00 pm Monday to Friday and 12:00 Noon on Saturdays and Sundays. Samples must reach the laboratory in Waterford Regional Hospital one hour before these above times.
Adult Single Daily Dosing Algorithm for Gentamicin

(Exclusions: Endocarditis & renal impairment. Caution required in CF patients, pregnant women & patients with severe burns.)

Is Creatinine Clearance (CrCl) >80ml/min?

\[ CrCl = (140 - \text{Age}) \times \text{Weight(kg)} \times (\text{Use ODW if BMI}>30)^* \times 1.23 \text{ (males)} \times 1.04 \text{ (females)} \]

Serum Creatinine(\text{umol/L})

**If anuric (<500mls/day), treat as CrCl<10ml/min**

- **Yes**
  - Give first dose of IV Gentamicin 5mg/kg* (based on Actual Body Weight or ODW if obese*). Record actual time of dose (Ideally 4-6pm). Dose should not exceed 500mg/day
  - Take blood for serum gentamicin level 16-18 hours after FIRST dose. Record actual time of sampling. (4pm dosing = 8-10am level, 6pm dosing = 10am-12noon level)

- **No**
  - CrCl(ml/min) Dose
    - 50-80 4mg/kg
    - 30-50 3mg/kg*
    - 10-30 2mg/kg*
    - <10 1-2mg/kg* redose when level <1µg/ml

Is trough level <1µg/ml

- **Yes**
  - Continue current regimen.
  - Repeat trough levels and serum creatinine concentration twice weekly (if renal function is poor/deteriorating and/or previous trough levels are high, then levels need to be checked more frequently e.g. daily)

- **No**
  - Check time dose was given and sample taken. Was level taken at 16-18 hours after dose?
    - **Yes**
      - Is trough level >1(µg/ml) but <2(µg/ml) and treatment still Indicated?
        - **Yes**
          - Reduce once daily dose by 1mg/kg*
        - **No**
          - Seek advice from Pharmacy or Clinical Microbiology
    - **No**
      - Redose when level <1µg/ml

*Weight used should be actual body weight (ABW) or for obese patients (BMI>30), an obese dosing weight (ODW) must be calculated.

\[ \text{ODW} = \text{IBW} + 0.4 (\text{ABW} - \text{IBW}) \]

Dose should never exceed 500mg.

BMI = Weight (kg)/Height (m)^2

IBW (males) Kg = 50 + (0.9 x no. of cm over 152cm)

IBW (females) Kg = 45.5 + (0.9 x no. of cm over 152cm)

1 foot = 30.5cm, 1 inch = 2.54cm
# Appendix 3: Glycopeptides: Vancomycin & Teicoplanin

## Vancomycin Dosage Schedule

<table>
<thead>
<tr>
<th>Levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collect predose level before 4th dose of vancomycin. Give the dose. Any adjustments necessary can be made to the 5th dose onwards. Predose level should be between 10-15µg/ml. (In severe/complicated infection 15-20 µg/ml). If continuing vancomycin and renal function is stable, repeat level twice weekly. Daily levels may be required if renal function is unstable. <strong>Note that 1-hour post dose levels are not necessary.</strong> Clearly state dose, time of dose and time of blood sample collection on the request form. At weekends routine assays are carried out at midday on Saturdays and Sundays.</td>
<td>Must be administered slowly IV at a maximum rate of 10mg/min to avoid reaction such as red man syndrome. In severe/complicated infections a loading dose of 25-30mg/kg can be used to facilitate rapid attainment of target trough serum vancomycin concentration. Complicated Infections: 1. Bacteraemia 2. Endocarditis 3. Osteomyelitis 4. Meningitis 5. Hospital Acquired Infections caused by Staph aureus</td>
</tr>
</tbody>
</table>

**Refer to dosing algorithm page 25.**

In severe/complicated infections a higher dose +/- loading dose to achieve pre-dose levels of 15-20 µg/ml may be required (see comments).

## Teicoplanin dosage schedule

<table>
<thead>
<tr>
<th>Levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>May be required in certain circumstances eg. endocarditis. Discuss with Microbiology team.</td>
<td>Renal impairment: If teicoplanin is to be used, the full dose is given for the first 4 days. Thereafter extended dosing intervals are required.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Levels</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mg/kg 12 hourly for 3 doses and thereafter once daily. Higher doses, 10-12mg/kg, in similar dosing schedule is indicated in serious infections eg. MRSA infections and endocarditis. Such patients should be discussed with the clinical microbiology team.</td>
<td></td>
</tr>
</tbody>
</table>

Guidelines for the empirical use of antimicrobials in adults HSE SE Hospitals June 2013 Revision Date June 2014 Revision no 7
**Dosing Algorithm for Vancomycin**

---

**Is Creatinine Clearance >60ml/min?**

- **Yes**
  - **CrCl = (140-Age) x Weight (ODW if BMI>30)* (kg) x 1.23 (male) or 1.04 (female)**
  - Serum Creatinine (\(\mu\)mol/L)
  - If patient is anuric (output <500mls/day), treat as per CrCl < 20ml/min

- **No**
  - **Give loading dose 25-30mg/kg (Actual body weight)**
  - **Give loading dose 15mg/kg (Actual body weight)**

---

**Check 1st level**

- **40-60**
  - **Dose**
  - **15mg/kg od**
  - **Before 3rd dose**

- **20-40**
  - **Dose**
  - **15mg/kg every 36-48 hrs.**
  - **Before 2nd dose**

- **<20**
  - **Dose**
  - **15mg/kg every 72-96 hrs.**
  - **Before 2nd dose. Hold dose until level available**

---

**Pre-dose level result**

<table>
<thead>
<tr>
<th>Level</th>
<th>Dose alteration</th>
<th>Recheck pre-dose level</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>Increase each dose by 250mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
<tr>
<td>10-15</td>
<td>Maintain dosing regimen</td>
<td>Twice weekly providing renal function is stable**</td>
</tr>
<tr>
<td>15-20</td>
<td>Reduce each dose by 250mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
<tr>
<td>&gt;20</td>
<td>Omit next dose and decrease each dose by 500mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
</tbody>
</table>

---

**Pre-dose level result**

<table>
<thead>
<tr>
<th>Level</th>
<th>Dose alteration</th>
<th>Recheck pre-dose level</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>Increase each dose by 500mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
<tr>
<td>10-15</td>
<td>Increase each dose by 250mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
<tr>
<td>15-20</td>
<td>Maintain dosing regimen</td>
<td>Twice weekly providing renal function is stable**</td>
</tr>
<tr>
<td>20-25</td>
<td>Reduce each dose by 250mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
<tr>
<td>&gt;25</td>
<td>Omit next dose and decrease each dose by 500mg</td>
<td>After adjusted dose given and before following morning dose**</td>
</tr>
</tbody>
</table>

---

**Withholding criteria**

- **>20**
  - Omit next dose and decrease each dose by 500mg

---

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
# Appendix 4: Treatment of Clostridium difficile Infection

## Initial Episode of CDI or First Recurrence

**General Measures:**
- Adequate replacement of fluid and electrolytes
- Immediately discontinue unnecessary antimicrobial therapy
- Avoid anti-motility medications
- Review other risk factors for CDI
- Review proton pump inhibitor use
- Appropriate infection prevention and control to include patient isolation with Contact Precautions and appropriate hand washing.

### Mild to Moderate CDI:
- No features of severe CDI
  - Oral or nasogastric metronidazole 400mg TDS for 10 to 14 days. (Grade A)
  - Inability to take oral medication: intravenous (IV) metronidazole 500mg TDS for 10 to 14 days. (Grade D)
  - Metronidazole intolerance or contraindication; oral vancomycin 125mg QDS for 10 to 14 days. (Grade A)
  - Oral fidaxomicin 200mg BD for 10 days may be an alternative to metronidazole (Grade C/D) or vancomycin (Grade A) in patients aged 16 yrs and older but only following discussion with a clinical microbiologist or specialist ID consultant.
  - Monitor closely for deterioration/progression to severe CDI

### Severe CDI:
- (Suggested by any of the following)
  - Clinical: fever, rigors, abdominal pain
  - Laboratory: Leucocytosis of ≥15,000 cells/μL, or rise in serum creatinine of ≥50% above baseline or serum creatinine >133 μmol/L.
  - Endoscopic findings: pseudomembranous colitis

### Severe, Complicated CDI:
- Severe disease with:
  - Hypotension
  - Shock
  - Rising serum lactic acid levels
  - Ileus
  - Megacolon

### Oral vancomycin 125 mg, QDS for 10 to 14 days. (Grade A)

- Early surgical opinion
- Vancomycin 500 mg, oral or nasogastric QDS and metronidazole 500mg, IV TDS (Grade D)
- Consider intracolonic vancomycin 500 mg, four to six times daily if ileus present or suspected (Grade D)

*Early surgical opinion*

### Fidaxomicin has not been tested in pregnant or breastfeeding women or in patients with a history of inflammatory bowel disease.*

Please refer to BNF for children or local paediatric formulary for doses of metronidazole and vancomycin for paediatric patients.

---

*Adapted From Surveillance, Diagnosis and Management of Clostridium difficile Infection in Ireland Update of 2008 Guidance HPSC 2013*
Figure R3: Management of Multiple Recurrences of CDI

First episode of recurrent CDI

Severity assessment, general measures and specific anti-CDI therapy as outlined in Figure R2

Second and subsequent episodes of recurrent CDI

- Review all anti-microbial therapy and other medications. Ensure adequate fluid and electrolytes and review nutritional status. (Grade D)
- Contact clinical microbiologist or specialist infectious diseases consultant expert for advice
- Consider the following options after expert advice as above:
  - Oral Vancomycin tapering/pulse therapy (Grade D):
    - 125mg 6 hourly for 7 days
    - 125 mg 12 hourly for 7 days
    - 125 mg daily for 7 days
    - 125 mg every other day for 7 days
    - 125 mg every 3 days for 7 days
  - Oral Fidaxomicin 200mg BD for 10 days (Grade D)
  - Oral Vancomycin 125mg QDS for 10 days followed by a chaser of oral rifaximin 400mg TDS for 20 days (Grade B)
  - Intravenous immunoglobulin therapy 150-400mg/kg per day for 1 to 3 doses (Grade D)
  - Faecal microbiota transplantation (Grade A)

Adapted From Surveillance, Diagnosis and Management of Clostridium difficile Infection in Ireland Update of 2008 Guidance HPSC 2013

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7 27
### Appendix 5: IV to PO Switch

Examples of choices of switch from IV to oral route

"Note: Oral Antimicrobials are significantly less costly than intravenous"

<table>
<thead>
<tr>
<th>IV</th>
<th>ORAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzylpenicillin 1.2 - 2.4g 4-6 hr</td>
<td>Amoxicillin 500mg 8 hr</td>
</tr>
<tr>
<td>Amoxicillin 1g 6 hr</td>
<td></td>
</tr>
<tr>
<td>Co-amoxiclav 1.2g 8 hr</td>
<td>Co-amoxiclav 625mg 8 hr</td>
</tr>
<tr>
<td>Clindamycin 600mg 6 hr</td>
<td>Clindamycin 300mg 6 hr</td>
</tr>
<tr>
<td>Clindamycin 1.2g 6 hr</td>
<td>Clindamycin 450mg 6 hr</td>
</tr>
<tr>
<td>Flucloxacillin 1 - 2g 6 hr</td>
<td>Flucloxacillin 500mg - 1g 6 hr 30 minutes before food</td>
</tr>
<tr>
<td>Clarithromycin 500mg 12 hr</td>
<td>Clarithromycin 500mg 12 hr</td>
</tr>
<tr>
<td>Metronidazole 500mg 8 hr</td>
<td>Metronidazole 400mg 8 hr</td>
</tr>
<tr>
<td>Ciprofloxacin 400mg 12 hr</td>
<td>Ciprofloxacin 500 - 750 mg 12 hr</td>
</tr>
<tr>
<td>Levofloxacin 500mg - 24hr/12hr</td>
<td>Levofloxacin 500mg - 24hr/12hr</td>
</tr>
<tr>
<td>Cefuroxime 750mg - 1.5g TDS 8 hr</td>
<td>Co-amoxiclav 625mg 8 hr In Penicillin Allergy discuss with Microbiologist</td>
</tr>
</tbody>
</table>
### Antimicrobials with Good Oral Bioavailability

*Sanford Guide 2010  
** Martindale 33rd edition  
*** Sanford Guide 2010 and Martindale 33rd edition

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Oral Bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>70-80%***</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>90%*</td>
</tr>
<tr>
<td>Fusidic Acid</td>
<td>91%(tablets)*</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>90%*</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>98%*</td>
</tr>
<tr>
<td>Linezolid</td>
<td>100%*</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>99%**</td>
</tr>
</tbody>
</table>
Appendix 6: Contingency Plan in Eventuality of Shortage of Intravenous Co-amoxiclav

**General Recommendations**

Consider using PO co-amoxiclav where co-amoxiclav is recommended for the indication and where PO route is clinically appropriate – refer to PO switch guidelines and Point 6 under General Guidance in Guidelines for Empiric Use of Antimicrobials in Adults.

**Do not substitute** IV piperacillin-tazobactam / IV ceftriaxone / cefotaxime / IV quinolones for IV co-amoxiclav where possible

**Refer to recommended alternatives** for each indication where IV co-amoxiclav features in the empiric and prophylaxis guidelines

**Practice the “Start Smart- Then Focus”** protocol for antimicrobial prescribing and the Surgical Prophylaxis Protocol diligently

**Specific Recommendations**

Recommended substitutes for IV co-amoxiclav by indication in HSE SE Guidelines for the empiric use of antimicrobials in the eventuality of unavailability of IV co-amoxiclav:

- **High Severity CAP** - IV cefuroxime 750mg - 1.5g TDS (plus PO clarithromycin)
- **Hospital Acquired Pneumonia within 4 days admission** - IV cefuroxime 750mg -1.5g TDS
- **Acute Exacerbation COPD** – Assess if PO co-amoxiclav or PO clarithromycin sufficient, if intravenous substitute needed - IV cefuroxime 750mg -1.5g TDS
- **Peritonitis, Diverticulitis Biliary Infections** – IV cefuroxime 750mg -1.5g TDS plus metronidazole
- **Pancreatitis (non-severe– first line)** - IV piperacillin-tazobactam cefuroxime 750mg -1.5g TDS plus metronidazole (IV severe / second line)
- **Human and animal bites** – Use PO co-amoxiclav where possible – if IV clinically indicated - IV cefuroxime 750mg -1.5g TDS plus metronidazole
- **Sinusitis, Otitis Media** – Use PO co-amoxiclav where possible – if IV clinically indicated - IV cefuroxime 750mg -1.5g TDS +/- metronidazole
Appendix 7: Relative Costs of Antimicrobials*

<table>
<thead>
<tr>
<th>COST OF ONE WEEK’S SUPPLY OF ANTIMICROBIALS</th>
<th>BASED ON NORMAL ADULT DOSE</th>
<th>(antifungals in bold italics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>€0-€10</td>
<td>Flucloxacillin PO, Metronidazole PO, Ciprofloxacin PO, Amoxicillin PO, Co-amoxiclav PO, Clarithromycin PO, Fosfomycin PO</td>
<td></td>
</tr>
<tr>
<td>€10-€40</td>
<td>Levofloxin PO, Amoxicillin IV, Metronidazole IV, Co-amoxiclav IV, Cefuroxime IV, Clindamycin PO, Fusidic acid PO, Ciprofloxacin IV, Vancomycin IV, <em>Fluconazole PO</em></td>
<td></td>
</tr>
<tr>
<td>€40-€60</td>
<td>Piperacillin-Tazobactam IV,</td>
<td></td>
</tr>
<tr>
<td>€150-€300</td>
<td>Clarithromycin IV, Levofloxacin IV, Rifampicin IV, Meropenem IV, Ceftriaxone IV, <em>Fluconazole IV</em></td>
<td></td>
</tr>
<tr>
<td>€300-€500</td>
<td>Acyclovir IV, Clindamycin IV,</td>
<td></td>
</tr>
<tr>
<td>€500-€1000</td>
<td>Linezolid PO &amp; IV, Ceftaroline IV,</td>
<td></td>
</tr>
<tr>
<td>€1000-€3000</td>
<td>Teicoplanin IV, Tigecycline IV, Fidaxomicin PO</td>
<td></td>
</tr>
<tr>
<td>&gt;€3000</td>
<td><em>Anidulafungin IV, Voriconazole IV, Amphotericin IV, Caspofungin IV</em></td>
<td></td>
</tr>
</tbody>
</table>

*Correct at time of publication.
**REFERENCES:**


11. Royal College of Obstetricians Green top guideline no 64A Bacterial Sepsis in Pregnancy.

12. HSE Adult Patient Observation Chart.

13. Surveillance, Diagnosis and Management of *Clostridium difficile* Infection in Ireland Update of 2008 Guidance HPSC 2013
HSE South East Acute Hospital Network Antimicrobial Stewardship Group Members

Microbiology Department WRH:

Microbiology SpRs

Dr. M. Hickey
Dr. M. Doyle
Dr. B. Carey
Ms. C. Troy, Surveillance Scientist

Pharmacy Departments:

WRH Antimicrobial Pharmacist
WGH Antimicrobial Pharmacist
SLKK/Kilcreene Antimicrobial Pharmacist
STGH Antimicrobial Pharmacist

Guidelines for the empiric use of antimicrobials in adults HSE SE Hospitals June 2013
Index no ASG 001 Date of Approval June 2013 Revision Date June 2014 Revision no 7
APPENDIX 2
BATES-JENSEN WOUND ASSESSMENT TOOL

Complete the rating sheet to assess wound status. Evaluate each item by picking the response that best describes the wound and entering the score in the item score column for the appropriate date. If the wound has healed/resolved, score items 1, 2, 3, & 4 as =0.

Location: Anatomic site. Circle, identify right (R) or left (L) and use "X" to mark site on body diagrams:
- Sacrum & coccyx
- Trochanter
- Ischial tuberosity

Shape: Overall wound pattern; assess by observing perimeter and depth.

<table>
<thead>
<tr>
<th>Item</th>
<th>Assessment</th>
<th>Date Score</th>
<th>Date Score</th>
<th>Date Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Size*</td>
<td>*0 = Healed, resolved wound 1 = Length x width &lt;4 sq cm 2 = Length x width 4--&lt;16 sq cm 3 = Length x width 16.1--&lt;36 sq cm 4 = Length x width 36.1--&lt;80 sq cm 5 = Length x width &gt;80 sq cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Depth*</td>
<td>*0 = Healed, resolved wound 1 = Non-blanchable erythema on intact skin 2 = Partial thickness skin loss involving epidermis &amp;/or dermis 3 = Full thickness skin loss involving damage or necrosis of subcutaneous tissue; may extend down to but not through underlying fascia; &amp;/or mixed partial &amp; full thickness &amp;/or tissue layers obscured by granulation tissue 4 = Obscured by necrosis 5 = Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Edges*</td>
<td>*0 = Healed, resolved wound 1 = Indistinct, diffuse, none clearly visible 2 = Distinct, outline clearly visible, attached, even with wound base 3 = Well-defined, not attached to wound base 4 = Well-defined, not attached to base, rolled under, thickened 5 = Well-defined, fibrotic, scarred or hyperkeratotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Undermining*</td>
<td>*0 = Healed, resolved wound 1 = None present 2 = Undermining &lt; 2 cm in any area 3 = Undermining 2-4 cm involving &lt; 50% wound margins 4 = Undermining 2-4 cm involving &gt; 50% wound margins 5 = Undermining &gt; 4 cm or Tunneling in any area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Necrotic Tissue Type</td>
<td>1 = None visible 2 = White/grey non-visible tissue &amp;/or non-adherent yellow slough 3 = Loosely adherent yellow slough 4 = Adherent, soft, black eschar 5 = Firmly adherent, hard, black eschar</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Necrotic Tissue Amount</td>
<td>1 = None visible 2 = &lt; 25% of wound bed covered 3 = 25% to 50% of wound covered 4 = &gt; 50% and &lt; 75% of wound covered 5 = &gt; 75% to 100% of wound covered</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 2

<table>
<thead>
<tr>
<th>Item</th>
<th>Assessment</th>
<th>Date Score</th>
<th>Date Score</th>
<th>Date Score</th>
</tr>
</thead>
</table>
| 7. Exudate Type | 1 = None  
2 = Bloody  
3 = Serosanguineous: thin, watery, pale red/pink  
4 = Serous: thin, watery, clear  
5 = Purulent: thin or thick, opaque, tan/yellow, with or without odor | | | |
| 8. Exudate Amount | 1 = None, dry wound  
2 = Scant, wound moist but no observable exudate  
3 = Small  
4 = Moderate  
5 = Large | | | |
| 9. Skin Color Surrounding Wound | 1 = Pink or normal for ethnic group  
2 = Bright red &/or blanches to touch  
3 = White or grey pallor or hypopigmented  
4 = Dark red or purple &/or non-blanchable  
5 = Black or hypopigmented | | | |
| 10. Peripheral Tissue Edema | 1 = No swelling or edema  
2 = Non-pitting edema extends <4 cm around wound  
3 = Non-pitting edema extends >4 cm around wound  
4 = Pitting edema extends <4 cm around wound  
5 = Crepitus and/or pitting edema extends >4 cm around wound | | | |
| 11. Peripheral Tissue Induration | 1 = None present  
2 = Induration, <2 cm around wound  
3 = Induration 2-4 cm extending <50% around wound  
4 = Induration 2-4 cm extending >50% around wound  
5 = Induration >4 cm in any area around wound | | | |
| 12. Granulation Tissue | 1 = Skin intact or partial thickness wound  
2 = Bright, beefy red; 75% to 100% of wound filled &/or tissue overgrowth  
3 = Bright, beefy red; <75% & >25% of wound filled  
4 = Pink, &/or dull, dusky red &/or fills <25% of wound  
5 = No granulation tissue present | | | |
| 13. Epithelialization | 1 = 100% wound covered, surface intact  
2 = 75% to <100% wound covered &/or epithelial tissue extends >0.5 cm into wound bed  
3 = 50% to <75% wound covered &/or epithelial tissue extends to <0.5 cm into wound bed  
4 = 25% to <50% wound covered  
5 = <25% wound covered | | | |

**TOTAL SCORE**

**SIGNATURE**

**WOUND STATUS CONTINUUM**

Plot the total score on the Wound Status Continuum by putting an "X" on the line and the date beneath the line. Plot multiple scores with their dates to see at-a-glance regeneration or degeneration of the wound.
Appendix 2

BATES-JENSEN WOUND ASSESSMENT TOOL
Instructions for use

General Guidelines:

Fill out the attached rating sheet to assess a wound’s status after reading the definitions and methods of assessment described below. Evaluate once a week and whenever a change occurs in the wound. Rate according to each item by picking the response that best describes the wound and entering that score in the item score column for the appropriate date. When you have rated the wound on all items, determine the total score by adding together the 13-item scores. The HIGHER the total score, the more severe the wound status. Plot total score on the Wound Status Continuum to determine progress.

Specific Instructions:
1. **Size**: Use ruler to measure the longest and widest aspect of the wound surface in centimeters; multiply length x width.
2. **Depth**: Pick the depth, thickness, most appropriate to the wound using these additional descriptions:
   - 1 = tissues damaged but no break in skin surface.
   - 2 = superficial, abrasion, blister or shallow crater. Even with, &/or elevated above skin surface (e.g., hyperplasia).
   - 3 = deep crater with or without undermining of adjacent tissue.
   - 4 = visualization of tissue layers not possible due to necrosis.
   - 5 = supporting structures include tendon, joint capsule.
3. **Edges**: Use this guide:
   - Indistinct, diffuse = unable to clearly distinguish wound outline.
   - Attached = even or flush with wound base, no sides or walls present: flat.
   - Not attached = sides or walls are present; floor or base of wound is deeper than edge.
   - Rolled under, thickened = soft to firm and flexible to touch.
   - Hyperkeratosis = callous-like tissue formation around wound & at edges.
   - Fibrotic, scarred = hard, rigid to touch.
4. **Undermining**: Assess by inserting a cotton tipped applicator under the wound edge; advance it as far as it will go without using undue force; raise the tip of the applicator so it may be seen or felt on the surface of the skin; mark the surface with a pen; measure the distance from the mark on the skin to the edge of the wound. Continue process around the wound. Then use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved.
5. **Necrotic Tissue Type**: Pick the type of necrotic tissue that is predominant in the wound according to color, consistency and adherence using this guide:
   - White/grey non-viable tissue = may appear prior to wound opening; skin surface is white or gray.
   - Non-adherent, yellow slough = thin, mucinous substance; scattered throughout wound bed; easily separated from wound tissue.
   - Loosely adherent, yellow slough = thick, stringy, clumps of debris: attached to wound tissue.
   - Adherent, soft, black eschar = soggy tissue: strongly attached to tissue in center or base of wound.
   - Firmly adherent, hard/black eschar = firm, crusty tissue: strongly attached to wound base and edges (like a hard scab).

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197
6. **Necrotic Tissue Amount:** Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved.

7. **Exudate Type:** Some dressings interact with wound drainage to produce a gel or trap liquid. Before assessing exudate type, gently cleanse wound with normal saline or water. Pick the exudate type that is predominant in the wound according to color and consistency. Using this guide:

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloody</td>
<td>Thin, bright red</td>
</tr>
<tr>
<td>Serosanguineous</td>
<td>Thin, watery pale red to pink</td>
</tr>
<tr>
<td>Serous</td>
<td>Thin, watery, clear</td>
</tr>
<tr>
<td>Puntent</td>
<td>Thin or thick, opaque tan to yellow</td>
</tr>
<tr>
<td>Foul Puntent</td>
<td>Thick, opaque yellow to green with offensive odor</td>
</tr>
</tbody>
</table>

8. **Exudate Amount:** Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to determine percent of dressing involved with exudate. Use this guide:

<table>
<thead>
<tr>
<th>Amount</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Wound tissues dry.</td>
</tr>
<tr>
<td>Scant</td>
<td>Wound tissues moist; no measurable exudate.</td>
</tr>
<tr>
<td>Small</td>
<td>Wound tissues wet; moisture evenly distributed in wound; drainage involves ≤ 25% dressing.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Wound tissues saturated; drainage may or may not be evenly distributed in wound; drainage involves &gt; 25% to ≤ 75% dressing.</td>
</tr>
<tr>
<td>Large</td>
<td>Wound tissues bathed in fluid; drainage freely expressed; may or may not be evenly distributed in wound; drainage involves &gt; 75% of dressing.</td>
</tr>
</tbody>
</table>

9. **Skin Color Surrounding Wound:** Assess tissues within 4cm of wound edge. Dark-skinned persons show the colors "bright red" and "dark red" as a deepening of normal ethnic skin color or a purplish hue. As healing occurs in dark-skinned persons, the new skin is pink and may never darken.

10. **Peripheral Tissue Edema & Induration:** Assess tissues within 4cm of wound edge. Non-pitting edema appears as skin that is shiny and taut. Identify pitting edema by firmly pressing a finger down into the tissues and waiting for 5 seconds, on release of pressure, tissues fail to resume previous position and an indentation appears. Induration is abnormal firmness of tissues with margins. Assess by gently pinching the tissues. Induration results in an inability to pinch the tissues. Use a transparent metric measuring guide to determine how far edema or induration extends beyond wound.

11. **Granulation Tissue:** Granulation tissue is the growth of small blood vessels and connective tissue to fill in full thickness wounds. Tissue is healthy when bright, beefy red, shiny and granular with a velvety appearance. Poor vascular supply appears as pale pink or blanched to dull, dusky red color.

12. **Epithelialization:** Epithelialization is the process of epidermal resurfacing and appears as pink or red skin. In partial thickness wounds it can occur throughout the wound bed as well as from the wound edges. In full thickness wounds it occurs from the edges only. Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved and to measure the distance the epithelial tissue extends into the wound.

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Dear Ms Saliba,

With reference to yesterday's meeting, the below proposal has been accepted by the Faculty University Research Committee and will be forwarded to UREC for approval.

Once this is done your protocol will come back to the Faculty were a letter of approval is issued from the Chairman, Dr Mario Vassallo.

Protocol 32/2013

The validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta

Thanks

Kind regards,

Angie

---

Angie Debono,
Secretary

Faculty Office
Faculty of Medicine and Surgery
University of Malta, Medical School
Block A, Level 0
Mater Dei Hospital
Msida MSD 2090
Tel: 23401879
L-UNIVERSITÀ TA’ MALTA
Msida – Malta
Skola Medika
Spitar Mater Dei

Ref No: 32/2013

Ms Claudine Saliba
48, Fatima
Triq ir-Rebbiegha
Ghaxaq GXQ 1052

Thursday, 09th May 2013

Dear Ms Saliba,

Please refer to your application submitted to the Research Ethics Committee in connection with your research entitled:

The validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta.

The University Research Ethics Committee granted ethical approval for the above mentioned protocol.

Yours sincerely,

Dr. Mario Vassallo
Chairman
Research Ethics Committee
14th April 2013

Dear Ms. Saliba,

With reference to the above-named study, this is to confirm that, on the basis of the documentation you submitted, from the MDH data protection point of view you have been cleared to proceed with your study.

You are requested to submit a copy of your findings to this office at the end of your study.

You are also kindly requested to call Ms. Nadine Buhagiar to fill in the appropriate Data Protection Form prior to your commencement of the study.

Please remember that in no way should you retain any personal details you obtain from your research and this should be destroyed at the end of your study and you should abide to the provisions of the Data Protection Act at all times.

Good luck with your study.

Kind regards,

Michael Gonzi
Data Protection Officer,
Mater Dei Hospital
Tel: (+356) 2545 5334
Email: datapro.mdh@gov.mt
14th March 2013

Mr. Schembri
Mater Dei Hospital
Msida, Malta

Dear Mr. Schembri

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

The Pharmacology and Clinical Pharmacology board has approved my dissertation title. I will be seeking permission in the near future from the University Research ethics committee.

I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc. Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com

Mr Mark Schembri
M.D. L.R.C.P. L.R.C.P.S. F.R.C.S
Consultant Surgeon
Mater Dei Hospital
14th March 2013
Ms. Wubbles
Mater Dei Hospital
Msida, Malta

Dear Ms. Wubbles

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc, Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com
14th March 2013

Mr. Gatt
Mater Dei Hospital
Msida, Malta

Dear Mr. Gatt

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on the end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
8Sc. Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com

Mr. Dennis Gatt
LRCP FRCS(Eng.) FRCS (Edin)
Reg No: 1574
Mater Dei Hospital
25th March 2013
Dr. Antoine Vella
St. Vincent DePaul Residence
Luqa, Malta

Dear Dr. A. Vella,

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc. Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com
25th March 2013

Dr. Joe Dimech
St. Vincent DePaul Residence
Luqa, Malta

Dear Dr. Joe Dimech,

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity, ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

The Pharmacology and Clinical Pharmacology board has approved my dissertation title. I will be seeking permission in the near future from the University Research ethics committee.

I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc. Podiatry
Mob: 7967120
email: claudinesaliba@gmail.com

[Signature]

[Approved]

16/4/13
25th March 2013

Dr. George Bugeja
St. Vincent DePaul Residence
Luqa, Malta

Dear Dr. G. Bugeja

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. A3PI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc. Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com

Appendix 3
Appendix 3

1st April 2013

Dr. Anthony Fiorini
St Vincent De Paul Residence
Luqa, Malta

Dear Dr. Fiorini

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

The Pharmacology and Clinical Pharmacology board has approved my dissertation title. I will be seeking permission in the near future from the University Research ethics committee.

I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc. Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com

Permission granted

Dr. Anthony Fiorini
MB ChB FRCP MD
Consultant Geriatrician

2/4/13
21st March 2013

Dr. Fiorentino

St. Vincent De Paul Residence

Luqa, Malta

Dear Dr. Fiorentino

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ASPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

The Pharmacology and Clinical Pharmacology board has approved my dissertation title. I will be seeking permission in the near future from the University Research ethics committee.

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Best Regards

Claudine Saliba

BSc. Podiatry

Mob: 79677120

email: claudinesaliba@gmail.com
1st April 2013

Dr. Peter Ferry
St Vincent De Paul Residence
Luqa, Malta

Dear Dr. Ferry

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ARPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

The Pharmacology and Clinical Pharmacology board has approved my dissertation title. I will be seeking permission in the near future from the University Research ethics committee.

I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba
BSc. Podiatry
Mob:79677120
email: claudinesaliba@gmail.com

Agree

Peter S. Ferry @ GOV.UK

211
22nd February 2013

Dr. Brian Farrugia

St. Vincent De Paul Residence

Luqa, Malta

Dear Dr. B. Farrugia

I am a first year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, halfway through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba

BSc. Podiatry

Mob: 79677120

e-mail: claudinesaliba@gmail.com
1st April 2013

Dr. Edward Bellia

St. Vincent De Paul Residence

Luqa, Malta

Dear Dr. Bellia

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba

BSc. Podiatry

Mob: 79677120

email: claudinesaliba@gmail.com

Appendix 3
14th March 2013

Prof. K. Cassar
Mater Dei Hospital
Msida, Malta

Dear Prof. Cassar,

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABPI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I am aware that I have to strictly adhere to ethical issues involved especially issues relating to informed consent and confidentiality.

I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards,

Claudine Saliba
BSc. Podiatry
Mob: 79677120
email: claudinesaliba@gmail.com
14th March 2013

Mr. Attard

Mater Dei Hospital

Msida, Malta

Dear Mr. Attard

I am a 1st year student reading for a Masters in Pharmacology and Clinical Pharmacology at the University of Malta. My dissertation study entails the validation of the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. This involves identifying a wound with an infection, taking a swab test for culture and sensitivity. ABI will be taken, and a wound assessment sheet will be used to assess the improvement of the lesion. Antibiotic treatment if required would be given according to the algorithm provided. The participant will be seen on 3 instances, prior to antibiotic treatment, half way through antibiotic treatment and on end of treatment. My sample will be chosen from the population sample attending at TVU clinic in Mater Dei Hospital Msida and at SVPR Hospital Luqa.

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I would like to ask for your permission in order to be able to conduct this study. Your help will be greatly appreciated.

Best Regards

Claudine Saliba

BSc. Podiatry

Mob: 79677120

e-mail: claudinesaliba@gmail.com
On 2/19/13 6:28 AM, "CLAUDINE SALIBA" <csal0002@um.edu.mt> wrote:

> Dear Dr. Bates- Jensen.

> My name is Claudine Saliba I am a Maltese Podiatrist, currently studying
> for my Masters degree at the University of Malta. My dissertation will be
> used to validate the guideline algorithm for the antibiotic
> treatment for infected lower limb wounds or ulcers provided by the
> Antibiotic Team at Mater Dei Hospital in Malta.

> An overview of my dissertation methodology includes, collecting
> individuals who present with an infected ulcer, take a Culture and
> Sensitivity test in order to identify organisms present in the wound, take
> an ABPI and then start treatment.

> In order to identify any improvement in the wound which is caused by the
> antibiotics prescribed, I will be using the Bates- Jensen Wound Assessment Tool available on line on
> http://www.geronet.med.ucla.edu/centers/borun/modules/Pressure_ulcer_preve
> ntion/puBWAT.pdf

> I would like to ask you whether you would allow me permission to use this
> tool for my study. It will be used on three instances, prior to
> commencement of treatment, half way through treatment and on end of
> treatment.

> Your help would be greatly appreciated. Hope to hear from you soon

> Best Regards

> Claudine Saliba
> Podiatrist
> University of Malta
Hi Claudine,
I am happy to provide you permission to use the Bates-Jensen Wound Assessment Tool in your study. I am attaching the most recent version here for your convenience. Good luck with your study and please let me know if I can be of any assistance. Thanks very much for your consideration of the BWAT.
Sincerely,
Barbara
Barbara Bates-Jensen PhD, RN, FAAN
Associate Professor
UCLA School of Nursing &
David Geffen School of Medicine, Geriatrics
5-954 Factor Bldg.
700 Tiverton Ave.
Los Angeles, CA 90095-6919
Cell: 626-437-8543 (preferred)
email: bbatesjensen@sonnet.ucla.edu
Wound REACH Foundation at
www.ouchrace.com

IMPORTANT WARNING: This email (and any attachments) is only intended for the use of the person or entity to which it is addressed, and may contain information that is privileged and confidential. You, the recipient, are obligated to maintain it in a safe, secure and confidential manner. Unauthorized redisclosure or failure to maintain confidentiality may subject you to federal and state penalties. If you are not the intended recipient, please immediately notify us by return email, and delete this message from your computer.
<table>
<thead>
<tr>
<th>Index Number</th>
<th>Age and Date of Birth</th>
<th>Wound Location</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

**Co-Morbidities:**
- Vascular Disease
- Diabetes
- Hypertension
- Thyroidism
- Kidney Disease
- Others:

**Allergies:**

**Medication:**
- Antihypertensives
- Diuretics
- Anti-Depressants
- Glycemic medication
- Insulin
- Antibiotics
- Others

**Treatment Plan Visit 1**

**Treatment Plan Visit 2**

**Treatment Plan Visit 3**
APPENDIX 5
Kunsens għall-pazjenti

Ms. Claudine Saliba
48, Fatima
Triq ir-Rebbiegħa
Għaxaq GXQ1052
Mob: 79677120
e-mail: claudinesaliba@gmail.com
22 ta' Frar 2013

Għażż Partecipant/ Relative/ Gwardjan,

Jiena studenta ta' l-ewwel sena, u qed nistudja għall- Masters f' Farmakoloġija u Farmakoloġija Klinika. Dan il-studju ser jkun użat sabiex jivvalida l-algoritmu għall-użu ta' l- antibijotici għall-infezzjonijiet f' feriti jew uċeri fis-sieq li ġle maħruġ min tim fl-isptar Mater Dei f'Malta.


Dan l-istudju ma jinvolvi l-ebda trattament straordinarju. Ma ser issir l-ebda ħsara lil min jipparteċipa f'dan l-istudju.

L-ebda pressjoni ma ser issirlek biex tlparteċipa f'dan l-istudju, iżda l-parteċipazzjoni tiegħek tkun apprezzata hafna. F'kaz li tkun tintieq tieqafl mil-parteċipazzjoni tiegħek f'dan l-istudju, dan tista' tagħmlu f'kull stadju ta' l-istudju, bili bi kaktiżjani fuq in-numru tal-mobile jew inkella l-email.

Dejjem Tieghek
Claudine Saliba

Firma

Isem: ____________________________
Data: ____________________________
Firma tas-superviżur: ____________________________
Firma tal-co-superviżur: ____________________________
Appendix 5

Informed Consent for Patients

Ms. Claudine Saliba
48, Fatima
Triq ir- Rebbiegha
Ghaxaq GXQ1052
Mob: 79677120
email: claudinesaliba@gmail.com
22nd February 2013

Dear Participant/ Relative/ Guardian,

I am a 1st year student, reading for a Masters in Pharmacology and Clinical Pharmacology. This study will be used to validate the guideline algorithm for the antibiotic treatment for Infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta.

The aim of this study is to identify whether the algorithm mentioned above is efficient in treating infections present in lower limb wounds or ulcers. I would like to confirm that confidentiality shall be strictly adhered to. Any personal information collected shall not be made public.

For the purpose of this study, an infection will be identified, a culture and sensitivity (C&S) test will then be obtained and analysed (there is a possibility that 2 C&S test may be taken). Then the ABI will be assessed, this implies taking a ratio for the blood pressure present in the hand and in the leg. Then, antibiotic treatment as advised by the algorithm shall be given. A wound assessment chart will be used to collect data regarding the wound and also to record data whether the wound improved when antibiotics where administered according to the algorithm. You will be asked to attend the clinic to be assessed for this study for three times. These include on commencement of the study, half way through the treatment and at the end of the treatment. Throughout the latter 2 visits, the wound assessment sheet will be used to obtain any data required.

This study will not involve any extraordinary treatment. There will be no harm when participating in this study.

No pressure would be made in order to participate in this study, but your participation would be greatly appreciated. Should you wish to quit participation in this study, this can be done at any time throughout the study, by contacting myself on the mobile number or email available on the top of the consent sheet.

Yours Truly,

Claudine Saliba
Podiatrist
I agree to take part in this study regarding the validation of the guideline algorithm for the antibiotic treatment for infected lower limb wounds or ulcers provided by the Antibiotic Team at Mater Dei Hospital in Malta. Any queries I had have been adequately answered. I understand that taking part in this study is my voluntary choice.

Your signature

Name: __________________________

Date: __________________________

Supervisor’s Signature: [Signature]

Co-Supervisor Signature: [Signature]
APPENDIX 6
<table>
<thead>
<tr>
<th>Index number</th>
<th>Risk and Severity</th>
<th>Total Number of organisms pre-clean</th>
<th>Total number of organisms post-clean</th>
<th>Decrease in number of organisms from pre-clean to post clean</th>
<th>Improvement Difference from Visit 1 to visit 3</th>
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