# Prevalence and antimicrobial susceptibility pattern of methicillin-resistant *Staphylococcus aureus* (MRSA) at Port Moresby General Hospital, Papua New Guinea: A retrospective study

Jamblyne Pamu

A thesis submitted to Auckland University of Technology for partial fulfilment of the requirements for the degree of Master of Health Science (MHSc)

February 2019

School of Clinical Sciences

Primary Supervisor: Dr Jed Montayre

Secondary Supervisor: Professor Eleanor Holroyd

# Abstract

**Background:** Methicillin-resistant *Staphylococcus aureus* is increasing rapidly worldwide and is a public health concern. Methicillin-resistant *Staphylococcus aureus* (MRSA)is an important organism that causes both hospital-acquired and community-acquired infections. Its prevalence varies geographically and in different hospital settings. MRSA is resistant to all penicillin, beta-lactams and the cephalosporin group of antibiotics. There is increased risk of infection, mortality and morbidity associated with methicillin-resistant *Staphylococcus aureus*.

**Purpose**: The purpose of this retrospective quantitative study is to document the prevalence and antimicrobial susceptibility patterns of MRSA using variables such as age, gender, specimen type, ward type, clinical infections and antibacterials used.

**Design:** This project is a retrospective quantitative study utilising a positivist philosophical worldview with an objectivist epistemology. The data were collected from registry books and from the database of the different specimens sent in to the clinical microbiology laboratory for microscopy, culture and sensitivity testing that were analysed prospectively from 2012 to 2016.All confirmed MRSA cases were recorded with their susceptibility patterns. Data were collected at the hospital microbiology laboratory in Port Moresby General Hospital, Papua New Guinea, for a period of three months.

The statistical treatment of data was aided by SPSS (version 25) employing descriptive and chi-square techniques.

**Results:** A total of 1,006 MRSA isolates were confirmed in the five years from 2012 to 2016. The overall prevalence of MRSA was 63.9%. 529 patients were males and 474 were females. The predominant age groups were 0-5 years with 39% of the total MRSA and 20-39 years old with 13%. Many samples were swabs from wounds and skin and soft tissue infections, followed by venous blood. Surgical wards had the highest frequency of MRSA (26.7%). The sensitivity patterns of MRSA were as follows: vancomycin, 96%; tetracycline, 93%; chloramphenicol, 79%; erythromycin, 68%; and septrin, 64%. Statistical significance of $p \leq 0.05$ was observed for the following

categorical variables and antibacterials: gender with chloramphenicol (*p=0.019*);clinical infections with erythromycin (*p=0.001*); and clinical infections with septrin (*p=0.001*).

**Conclusion:** The high prevalence of MRSA as found prompted a need for effective control measures and continued surveillance at the Port Moresby General Hospital, Papua New Guinea. With the significance of the sensitivity patterns, a continued antimicrobial surveillance and strict policies for empirical treatment should be created as well. Overall effective infection control policies and antimicrobial stewardship programmes need to be implemented, evaluated regularly and maintained.

# Table of Contents

# List of Figures

# List of Tables

# Attestation of Authorship

"I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning."

Signature: Date:22 /02/2019

# Acknowledgements

The completion of this thesis would not have been possible if it were not for the following people and organisations:

Firstly, I would like to thank the Heavenly Father for his wisdom, knowledge and understanding bestowed on me during my study here in Auckland University of Technology (AUT) for two years.

Secondly, I would like to extend my deepest appreciation and gratitude to my primary supervisor Dr Jed Montayre for his support, guidance and knowledge throughout this journey. Without him correcting me and guiding me I would not have completed. He has helped me understand the research process, which is an achievement for me.

I would like to thank my secondary supervisor Professor Holroyd for her guidance throughout this thesis journey.

My extended thank you and appreciation goes to the New Zealand Government through the Ministry of Foreign Affairs and Trade for the award of a scholarship which enabled me to come study in New Zealand. The ever-wonderful scholarship officers at AUT, namely, Margaret, Sacha, Petrina and Prerna, who have guided and assisted me throughout this journey, I wholeheartedly appreciate all your efforts.

Lastly, but not the least, I would extend my warm gratitude to the Port Moresby General Hospital management and the Pathology Laboratory management for granting me the approval to collect data at the microbiology laboratory. A huge thank you as well to my colleagues in microbiology laboratory for their kind gestures towards me during my data collection period.

Finally, I would like to thank my family and my friends who have made life bearable through stressful days here in Auckland. To my wonderful dearly beloved parents who are up in heaven, I know they would have been so proud of me.

Thank you all!

Whakawhetai Koe!!

# Chapter 1 Introduction

## 1.1 Introduction

Data from several studies reported worldwide that methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the cause of hospital-acquired infections (HAIs) (Cosgrove et al., 2005; Engemann et al., 2003; Maragakis, Perencevich, & Cosgrove, 2014; Pai, Rao, & Rao, 2010).MRSA is a dangerous bacterium that is difficult to treat in humans because it is hard to diagnose and is resistant to penicillin-related antibiotics (Centres for Disease Control and Prevention [CDC], 2013b; Kesah et al., 2003; World Health Organization, 2014a). Therefore the economic burden of HAIs caused by drug-resistant micro-organisms, including MRSA, is greater than that for infections caused by other micro-organisms that are not drug resistant (National Nosocomial Infections Surveillance [NNIS], 2004; Stone, 2009).

The consequences associated with hospital-acquired MRSA (HA-MRSA) are two-fold. They cause infections that are fatal or prolong hospital stay and increase healthcare costs (Dilnessa & Bitew, 2016; Health Protection Agency [HPA], 2013; World Health Organization, 2006, 2014a).Firstly, the fatal infections that are caused by MRSA include bacteraemia (infection of the blood), osteomyelitis (bone infection) and endocarditis (infection of the endocardium) to name a few. Secondly, even when not fatal, MRSA causes patients longer hospitalisation, thus putting a financial strain on the hospital for their care and treatment (Dilnessa & Bitew,2016).

Methicillin-resistant *Staphylococcus aureus* has a varying prevalence and susceptibility profile in healthcare settings around the world (Centres for Disease Control and Prevention, 2010; Health Protection Agency [HPA], 2010).In developed countries such as the United Kingdom, Australia and New Zealand, MRSA prevalence rates have been reduced over the years (Boyce et al., 2005; Nimmo et al., 2007). In a developing nation such as Papua New Guinea, the status of MRSA is unknown. By documenting the prevalence of MRSA, prevention practices may be developed (Jarvis, Jarvis, & Chinn, 2012). The National Health Plan in Papua New Guinea aims to improve preparedness for disease outbreaks, therefore documenting the prevalence and antimicrobial susceptibility profile of disease-causing agents, such as MRSA, will help contribute to this key result area (National Department of Health [NDOH], 2010). This also aligns

with the Papua New Guinea Vision 2050 of a healthy and happy Papua New Guinea society by 2050 (The Independent State of Papua New Guinea, 2012).

## 1.2 MRSA infections: A global concern

Methicillin-resistant *Staphylococcus aureus* is a dangerous multi-drug resistant micro-organism and has become a global health problem (Boucher & Corey, 2008; Diekema et al., 2004; Gad, El-Gafaar, El-Domany, & Hashem, 2010; Grundmann et al., 2010; Jones et al., 2002; Pai et al., 2010). The prevalence of MRSA varies in hospitals and communities worldwide. The prevalence across regions ranges from 10-40% in Australia and New Zealand, 20-70% in the South-east Asian nations and 20-40% in African regions (Chen & Huang, 2014; Coombs et al., 2009; Falagas, Karageorgopoulos, Leptidis, & Korbila, 2013; Institute of Environmental Science and Research [IESR], 2012). The European and American regions have reported prevalence rates of 20-40% (Bouchiat et al., 2015; Centres for Disease Control and Prevention [CDC], 2014; Moet, Jones, Biedenbach, Stilwell, & Fritsche, 2007).

### 1.2.1 MRSA resistance

Methicillin-resistant *Staphylococcus aureus* is resistant to penicillin groups of antibiotics, cephalosporins and all other beta-lactams, thus giving rise to many consequences (Boyce et al., 2005).This makes treatment of MRSA difficult and places financial constraints on hospitals which need to acquire third-generation antibiotics to treat it. In high income countries the trend of infections due to MRSA in hospitals is different to that in low-to-medium income countries (Organisation for Economic Co-operation and Development [OECD], 2016).For high income countries, it is easier to purchase new antibiotics and there are effective infection control measures; however, for the low-to-medium income countries, the burden of disease is high and higher antibiotics are expensive and not easily accessible (Organisation for Economic Co-operation and Development [OECD], 2016).

## 1.3 Antibiotic and antimicrobial resistance in OECD and developing countries

The World Health Organization (2018) defined antibiotic resistance as the change in response to antibiotics by bacteria. Antimicrobial resistance occurs when micro-organisms develop resistance to the antimicrobials they are exposed to (Organisation

for Economic Co-operation and Development [OECD], 2016). Developing countries and the countries who are members of the OECD have all created strategies to combat this ever-increasing problem of antimicrobial resistance. The OECD (2016) has created effective policies that helped curb and reduce the increase of antimicrobial resistance. These policies include: guidelines on the rational use of antimicrobials for prophylaxis nationwide; implementation of antimicrobial stewardship programmes; strategies to rationalise the use of antimicrobials; and putting monitoring systems in place for antimicrobial consumption (Organisation for Economic Co-operation and Development [OECD], 2016). The OECD found that the best strategy to reduce the inappropriate use of antibiotics is education and information awareness in the general population including medical doctors. These strategies came about when the OECD carried out a survey on HAIs in their member countries, including MRSA. They were able to gather data from these countries to come up with policies to reduce the spread of multi-drug resistant organisms, mainly MRSA, *Escherichia coli* and *Streptococcus pneumoniae*.

The developing nations, mainly in the Asia-Pacific region and the African continent, have reported high prevalence rates of MRSA both in hospitals and in communities(Chen & Huang, 2014; Dilnessa & Bitew, 2016; Falagas et al., 2013). Researchers have found varying reasons as to why MRSA prevalence was high in developing countries (Alrabiah, Alola, Banyan, Al Shaalan, & Al Johani, 2016; Bell & Turnidge, 2002; Chen & Huang, 2014; Molton, Tambayah, Ang, Ling, & Fisher, 2013). These reasons were: ineffective infection control policies; lack of monitoring and surveillance of antibiotic use; and over-prescribing of antibiotics. The developing countries employed different strategies to help reduce HAIs caused by MRSA; however, the results vary geographically and across different hospital settings. The recommendations emerging from the cited studies were for on-going surveillance, infection control measures and effective antimicrobial stewardship programmes as the solutions to reducing HAIs caused by MRSA (Akpaka, Kissoon, Swanston, & Monteil, 2006; Bouchiat et al., 2015; Pai et al., 2010; Rajaduvaipandi et al., 2006; Tiwari, Das, Sapkota, Sivarajan, & Pahwa, 2009).

## 1.4 Background information of Papua New Guinea

Papua New Guinea is the largest Island in the Pacific. It is located north of Australia. It has a land mass of 452,860 $km^2$(Papua New Guinea's information, n.d.). The

population of Papua New Guinea is approximately eight million(Papua New Guinea's information, n.d.). It has an annual population growth rate of 3.1% (National Statistical Office [NSO], 2011). Papua New Guinea has 22 provinces and is divided into four regions: Southern, Momase, Highlands and Islands. According to 2017 statistics, 13.09% of people live in urban areas (The Statistical Portal, n.d.). Most of the people, estimated to be more than 75% still live in rural areas. There are over 800 languages spoken in Papua New Guinea. Papua New Guinea has a very diverse culture.


*Figure 1*: Map of Papua New Guinea.Source: (Wikipedia, n.d.-a).

Papua New Guinea (see Figure 1) sits just to the south of the equator and has a hot, humid climate. It is a tropical country and has two seasons, wet and dry. The northwest monsoon season is from December to March while the southwest monsoon is from May to October (Papua New Guinea's information, n.d.). The highlands region of Papua New Guinea experiences the highest rainfall, ranging from 2000 to 5000 mm annually. It is largely mountainous and most of it is covered with tropical rainforests. The vegetation in Port Moresby and the whole of the National Capital District is mainly savannah grassland. In Port Moresby the temperatures range from 26˚C to 28˚C annually.

Papua New Guinea broke away from Australian colonisation and became an independent nation on September 16, 1975. Papua New Guinea has a growing economy that is built on its natural resources such as gold, copper ore, crude oil and gas. The agriculture, forestry and fishing industries help boost the economy too.

## 1.5 Personal context

I am a medical laboratory scientist by profession. I have been working in the microbiology laboratory of Port Moresby General Hospital for six years before pursuing further studies. On occasions there were outbreaks of MRSA; however, the infection control unit of the hospital lacked proper systems and processes to respond to these outbreaks. Therefore, I feel the need to document and record the prevalence of MRSA and investigate to see if it is increasing at my hospital and whether it is as alarming as recorded in the literature on most developing nations.

## 1.6 Healthcare system in Papua New Guinea

A healthcare system is a complex system that involves many processes. It involves "all the activities whose primary purpose is to promote, restore or maintain health''(The World Health Report, 2000). Some developing countries have on occasions run low on medical supplies. Papua New Guinea shares a similar situation to other developing nations. Healthcare in Papua New Guinea is primarily provided by the government and church-run facilities. It is funded by a combination of tax revenues, donors and the user (WHO Western Pacific Region, 2018).

Papua New Guinea's health system is struggling to improve. The country has the highest incidence of HIV and AIDS in the Pacific region and the fourth highest in the Asia-Pacific region (Papua New Guinea's information, n.d.). The burden of disease is high, and the costs associated with health are enormous. Maternal, child health and infectious diseases currently account for the highest mortality rates among Pacific Island nations and put a tremendous strain on the provision of health services (National Department of Health [NDOH], 2010).According to a report, antimicrobial resistance has become problematic in Papua New Guinea (Ferguson, 2015; World Health Organization, 2014a). Tuberculosis (TB) is becoming multi-drug resistant in Papua New Guinea and is putting a strain on the government in terms of treatment costs (Aia et al., 2016; World Health Organization, 2015).Papua New Guinea has the highest incidence rates of TB in the Western Pacific Region (Aia et al., 2016; Ley, Riley, & Beck, 2014).

Despite Papua New Guinea being a country that has a high burden of both communicable and non-communicable diseases, there are no documented reports

regarding the prevalence and antimicrobial profile of MRSA. Nonetheless, as reported across developing nations, the mortality and morbidity associated with MRSA are significantly high (Beam & Buckley, 2006; Cosgrove et al., 2005; Dilnessa & Bitew, 2016; Kejela & Bacha, 2013; Klevens et al., 2007; Pai et al., 2010). Whilst some developing countries still have high MRSA prevalence rates in their hospitals despite having continuous surveillance and preventative measures in place, Papua New Guinea may share similar or different trends. According to the National Health Plan, one of the key result areas is to have preparedness for outbreaks when they occur, and having this policy in place will ensure that a hospital is well prepared to deal with HAIs(National Department of Health [NDOH], 2010). This in turn aligns with the vision 2050 for Papua New Guinea (The Independent State of Papua New Guinea, 2011).

Papua New Guinea is struggling in healthcare service delivery. That includes human resources and medical supplies. There are health disparities. The ratio of doctors to people is 1:20,000 (National Department of Health [NDOH], 2010). This is a far cry from 1:155 doctors to people in Cuba and 1:396 in the Unites States of America (WHO,2011;Cuba and the Global Health Workforce,2019).Those living in rural areas do not have easy access to health services. Due to Papua New Guinea's rugged terrain, it is most difficult to transport patients to major hospitals and many patients die whilst travelling on foot to seek proper health care.

## 1.7 Research questions

There are currently no documented reports of the prevalence and antimicrobial susceptibility profile of MRSA at Port Moresby General Hospital, Papua New Guinea. The questions this research seeks to answer are:

1. What is the prevalence of confirmed methicillin-resistant *Staphylococcus aureus* among *Staphylococcus aureus* isolates?
2. What is the antimicrobial susceptibility profile of methicillin-resistant *Staphylococcus aureus* isolated from all sites in Port Moresby General Hospital?
3. Is there a significant association between antibacterial sensitivity or resistance to patient's profile (age and gender)?

## 1.8 Purpose of study

This Master's project aims to document the prevalence and antimicrobial susceptibility profile of MRSA in Port Moresby General Hospital, Papua New Guinea. It will be used as evidence to prioritise prevention measures against MRSA. It is a retrospective quantitative study that gathered data on confirmed methicillin-resistant isolates from Port Moresby General Hospital over a five-year period, from 2012 to 2016.

To date there are no current statistics on the prevalence and antimicrobial susceptibility of MRSA in Port Moresby General Hospital, Papua New Guinea. This is the first study to be conducted on this topic. The findings from this study will provide a basis for recommendations for better ways of treating and putting in place strict control and preventative measures for MRSA infections in the hospital. The findings will enable the creation of an antimicrobial profile for MRSA in Port Moresby General Hospital in Papua New Guinea. According to WHO reports, Papua New Guinea has high and increasing number of multi-drug resistant organisms (MDROs), which includes MRSA (World Health Organization, 2014c). By having the results of this research project in place, the hospital will be able to create strict measures for reducing MDROs in Port Moresby General Hospital. The prevalence of MRSA causing infections and deaths varies around the world (Hassoun, Linden, & Friedman, 2016). Papua New Guinea may share similar or have different trends when compared to other countries in terms of MRSA prevalence and epidemiology; however, due to the gaps in the literature, the prevailing situation in the country is unknown.

## 1.9 Thesis structure

This thesis is presented in six chapters.

*Chapter one: Introduction*. This chapter introduces the research topic, its significance, the background information about Papua New Guinea, the research setting, researcher's background, and the healthcare system in Papua New Guinea. It discusses the significance of HAIs caused by MRSA and the importance of documenting the prevalence and antimicrobial profile of MRSA.

*Chapter two: Literature review*. This chapter reviews literature relevant to the research topic. Most of the literature reviewed was from the 1990s onwards. The literature

review mainly focused on the prevalence of MRSA in hospital settings worldwide and the susceptibility profile of MRSA. The scope of search included infection control measures, epidemiology and government health strategies for the reduction of MRSA in health settings in both developed and developing countries.

*Chapter three: Methodology and methods*. This chapter discusses the theoretical framework and practical methods employed in this research. The significance of using the positivist approach and methodology is discussed and the approach is justified. The ethics process and approvals are discussed. The statistical techniques employed in this study are descriptive statistics and the chi-square test of independence, using the statistical software SPSS version 25. These techniques are discussed and justified in this chapter.

*Chapter four: Results*. Chapter four of this study presents the results in tables and graphs after analysis of the data using SPSS version 25. The results are interpreted using international references where needed.

*Chapter five: Discussion*. This chapter interprets and summarises the significance of the findings in terms of the two research questions. It examines the results, makes comparisons with existing literature and, where possible, justifies the findings.

*Chapter six: Conclusion*. This chapter summarises the thesis, points out the strengths and limitations of this research in relation to the results and discussions previously presented.

# Chapter 2 Literature Review

## 2.1 Introduction

This chapter presents a critical review of the literature regarding MRSA prevalence and antibiotic susceptibility patterns in hospitals. The purpose of this review is to report and review literature from both developed and developing nations. This chapter critiques and discusses the global epidemiological trend of MRSA as per the literature that was retrieved.

Finally, this review comments on the existing gap in literature in relation to Papua New Guinea and considers where Papua New Guinea lies in terms of prevalence and antimicrobial susceptibility.

## 2.2 Search strategy

Published studies were identified electronically using the following search engines:EBSCO (CINAHL complete and via MEDLINE), Google Scholar, PUBMED,and Scopus. The retrieved articles were published between the 1990s and 2018; however, the focus was on recently published articles from 2012 to 2018.Those years were chosen because of the years that data was collected. Medicine changes all the time, therefore to have recent articles would give validity to this research project.

The following key search terms were used: antibiotic resistance, hospital-acquired infections, MRSA prevalence, MRSA surveillance AND antimicrobial profile, MRSA AND infection control, Staphylococcus aureus.

More than 200 studies were retrieved from the electronic databases and reviewed. A total of approximately 100 items among the 200 of literature were retrieved from Google Scholar. A manual search on google for literature was also done, which mainly included webpages. The inclusion criteria for literature reviewed were focused around the title, theoretical framework and methodology. The titles of the studies selected included the following terms: antimicrobial resistance, antimicrobial susceptibility patterns of MRSA, colonisation of MRSA, HAIs, epidemiology of MRSA, MRSA infections, and prevalence of MRSA. Under the theoretical framework, selected studies included positivist and post-positivist philosophical worldviews. Under the

methodology/procedure section, the selected studies were prospective and retrospective studies. The methods of antimicrobial susceptibility testing techniques reviewed included: E-tests, Kirby-Bauer disc diffusion, minimal inhibitory concentration(MIC), molecular typing and polymerase chain reaction (PCR).The studies that were excluded were those reporting prevalence of antimicrobial susceptibility patterns of MRSA from animals and animal products.

## *2.3 Staphylococcus aureus*

*Staphylococcus aureus* is a type of bacteria that about 33% of healthy people carry in their skin and nasal cavities (Baird, 1996; Centres for Disease Control and Prevention, 2010; Cosgrove et al., 2005; Perry et al., 2004). *Staphylococcus aureus* causes infections such as skin, soft-tissue, respiratory, bone, joint and endovascular disorders in healthcare settings and these infections can be fatal (Dilnessa & Bitew, 2016; Health Protection Agency [HPA], 2010, 2013; World Health Organization, 2006). However, when isolated in a diagnostic laboratory, *Staphylococcus aureus* was noted to be sensitive to the methicillin group of antibiotics (Centres for Disease Control and Prevention,2010). Despite this sensitivity, there is an increasing incidence of methicillin-resistant *Staphylococcus aureus,* which is a growing subtype of the *Staphylococcus* family. This poses a significant threat due to its resistance to the commonly available penicillin group of antibiotics (Kesah et al., 2003). It is, nevertheless, easier to treat methicillin-sensitive *Staphylococcus aureus* (MSSA) than MRSA. However, MRSA produces the enzyme beta-lactamase that creates a resistance to most beta-lactams, cephalosporins, penicillin, carbapenems and cephamycin (Chambers, 2001; Knight et al., 2012).

## 2.4 MRSA:History and prevalence

*Staphylococcus aureus* was an organism that existed for over a billion years, until 50 years ago it was recognised as a bacteria causing disease in humans (Moellering, 2012)..MRSA is any strain of Staph aureus bacterium that is resistant to a large group of beta lactam antibiotics (Raygada & Levine,2009). Both MSSA and MRSA produce the enzyme penicillase. MRSA was first discovered in 1961 in the United Kingdom, two years after the introduction of methicillin. However, others dated its first appearance to between 1940 and 1950 (Stefani & Gogilo, 2010). The discrepancy of the different dates was due to overuse and misuse of penicillin that gave rise to MRSA in different

settings. It was then reported in the European countries,Japan,Australia and United States of America (C. Enright et al., 2002; M. C. Enright, 2003).MRSA has since spread rapidly worldwide. However, there is scant data regarding its first appearance in Papua New Guinea or the other Pacific Islands countries.

MRSA is considered one of the significant gram-positive pathogens (Ronald, 1967, 2001). The other two gram-positive pathogens are multi-drug resistant *pneumococci* and vancomycin-resistant *enterococci*. They are dangerous and are known to cause morbidity and mortality in hospitals. MRSA is categorized as a multi-drug resistant organism (MDRO) as it is resistant to most antibiotics.

MRSA is reported to be carried by 2%of any healthy population (Centres for Disease Control and Prevention, 2010; Centres for Disease Control and Prevention [CDC], 2013b). It has become a global health problem (Appelbaum, 2006; Chen & Huang, 2014; Falagas et al., 2013; Goethebeur, Landry, Han, & Vicente, 2006; Pai et al., 2010; Rajaduvaipandi et al., 2006). Countries with the highest rates of MRSA are the United States, Canada, Japan and Indonesia, and also Northern European countries (World Health Organization, 2013). MRSA is widely recognized as the causative pathogen for hospital-acquired and community-acquired infections (Centres for Disease Control [CDC], 2017; Sit et al., 2017).

A patient is susceptible to being infected with MRSA only when there is a break or wound in the skin or when the patient's immune system is weakened (Centres for Disease Control and Prevention, 2010; World Health Organization, 2014a).Furthermore HA-MRSA is associated with underlying medical comorbidities; such as ventilator-associated and hospital associated pneumonia, surgical site infections, as well as catheter-related infections (Raygada & Levine, 2009)

The prevalence of MRSA varies in hospitals according to geographical settings (Anupurba et al., 2003).In the European countries, MRSA prevalence in hospitals ranges from less than 5% to more than 25% (Bouchiat et al., 2015; European Centre for Disease Prevention and Control [ECDCP], 2018; European Centre for Disease Prevention and Control [ECDPC], 2013). However, Gould (2008) documented a significant upward trend of MRSA in other European countries such as Belgium, Denmark, Finland, Holland and Portugal. It was also reported that MDROs including

MRSA are mainly found in hospital settings rather than in the community (Chambers, 2001).

Previous studies in the United States by Bauer et al. (2010) reported varying trends in the prevalence of MRSA. Boucher and Corey (2008) reported an increase of MRSA compared to other organisms in various United States hospitals. They reported that MRSA accounts for more than 60% of all pathogenic organisms in US hospitals. However, there are conflicting results that have been reported regarding prevalence of MRSA in the United States (Goethebeur et al., 2006). Appelbaum (2006) reported the prevalence of MRSA in the United States as ranging from 33%-55%. Another study reported a prevalence range of 33.1 % to 45.7% among in-patients in 33 hospitals in the US (Jones et al., 2002).Despite the varying trends that have been documented, the prevalence of MRSA as discussed also seem to be increasing at a rate of five percent to ten percent in the United States over a period of four years (Appelbaum,2006;Jones et al.,2002). This also implies that the prevalence of MRSA varies geographically in the United States (Centres for Disease Control and Prevention [CDC], 2018; Cosgrove et al., 2005).

In contrast, the Centres for Disease Control and Prevention [CDC] (2014)reported a decline in HA-MRSA in the United States from the years 2005 to 2011.This is based on an overall report that was captured in a national surveillance programme by the Centre for Disease Control and Prevention.

MRSA prevalence rates across the world ranged from approximately 2% to 70 % (Nickerson, West, Day, & Peacock, 2009; World Health Organization, 2014b).The prevalence of HA-MRSA is reported to be highest (28%-70%) across the Asian region, where it is the highest in the world (Chen & Huang, 2014). According to Bell and Turnidge (2002) and Chen and Huang (2014), the highest prevalence rates of HA-MRSA were recorded in the Asia-Pacific region. Papua New Guinea is situated in the Asi-Pacific region. National MRSA prevalence surveillance carried out in New Zealand reported an increase of 20%-50% of MRSA in hospitals over 10 years (Heffernan & Bakker, 2016). To date, a lot of preventative measures have been implemented to combat the rise of HA-MRSA. A few examples of these preventative measures include; cleanliness of healthcare providers' hands using soap and water or alcohol based

hand rubs prior to and after attending to a patient, cleanliness of hospital rooms and medical equipment, contact precautions used when caring for patients with MRSA,and control of the use of antimicrobial agents (CDC,2017). All these preventative measures were trialled and assessed. The most effective preventative measure was the usage of alcohol based hand rubs (CDC,2017;WHO,2013). All these preventative measures coupled together with continuous monitoring may prove effective and help reduce HA-MRSA.

## 2.5 Mechanism of MRSA resistance to antimicrobial agents

Antimicrobial resistance worldwide has compromised treatment. MRSA is considered one of the most problematic MDROs because it has developed resistance to most antibiotics (Alekshun & Levy, 2007; Appelbaum, 2007).It is therefore vital to understand the resistance mechanisms of dangerous pathogens such as MRSA in order to be able to develop new antimicrobial agents to cure infections caused by these pathogens. Generally, all bacteria develop intrinsic and acquired resistance mechanisms to antibiotics. Intrinsic mechanisms occur when bacteria develop resistance naturally to antibiotics, while acquired mechanisms occur when bacteria become resistant to antibiotics that they were previously sensitive to (Tenover, 2006).

There are two mechanisms for the resistance of MRSA. Firstly, *Staphylococcus aureus* produces beta-lactamase, an enzyme which prevents or slows the affinity of the penicillin group of antibiotics (Appelbaum, 2007; Mulligan et al., 1993). Secondly, it creates an alteration in membrane bound-enzymes called penicillin-binding proteins (PBPs). The PBPs' function is to enable the survival of the bacteria, and they are targeted by beta-lactam antibiotics. Haddadin, Fappiano, and Lipsett (2002)stated further that MRSA is mediated by the mecA gene that encodes a single added PBP, known as PBP2a, which has a low affinity for all beta-lactams. However Hiramatsu, Katayam, Yuzawa, and Ito (2002) found that having this mecA gene alone does not predict total resistance to methicillin, and that some strains are still susceptible to methicillin. Therefore, correctly identifying strains will enable proper treatment protocols. What is worrisome is that most developing countries are a long way from acquiring the sophisticated technologies needed to correctly identify strains of pathogenic organisms. Access to technologies such as PCR would make it possible to correctly identify different strains of MRSA.

Understanding the antimicrobial mechanism of pathogens and testing against different antimicrobial agents to ascertain the sensitivity patterns will enable clinicians to correctly treat patients. This will help reduce antibiotic resistance as well.

Not all strains of *Staphylococci* may give off sensitive results to antibacterials tested in the laboratory. Different methods of antimicrobial sensitivity testing for MRSA yield varied results. In-vitro susceptibility testing or molecular (PCR) would give correct patterns of antimicrobial susceptibility for MRSA (Stratton,2006).Furthermore in vitro or molecular susceptibility testing would give rapid detection and confirmation of carriage states of epidemiologically and clinically important pathogens like MRSA. This would also guide clinicians on antimicrobial selection in the treating of patients (CLSI,2012).However, others opposed in-vitro susceptibility testing as a means of providing better clinical outcomes in certain infections caused by gram-positive organisms (Apparao, Ruegg ,Lago,Godden,Bey & Leslie,2009). The conventional methods of testing, which include disc diffusion and MIC, are still widely applied in clinical settings; however in-vitro testing is preferred for the analysis of recurring infections and to identify optimal treatment approaches (Mulligan et al., 1993). Since antimicrobial resistance is increasing, such sophisticated methods should be employed. However, the costs of doing in-vitro testing is enormously high particularly for a developing nation like Papua New Guinea.

## 2.6 Susceptibility of MRSA to various antibiotics, and MRSA strains and breakpoints

MRSA shows different sensitivity patterns to different antimicrobials across different healthcare settings (Chen & Huang,2014). The treatment methods and guidelines used are dependent on the type of antimicrobial susceptibility guidelines from the laboratory. According to Centres for Disease Control and Prevention [CDC] (2013b) and World Health Organization (2014d) reports, MRSA is generally resistant to first-line antibiotics. However, they are sensitive to carbapenems and cephalosporins. Furthermore, MRSA shows sensitivity to the named antibacterials: chloramphenicol,ciprofloxacin,clindamycin,erythromycin,gentamycin,nitrofurantoin, oxacillin,tetracycline,trimethoprim-sulphamethoxazole (SXT), and vancomycin (Wernitz et al., 2005).Despite the known sensitivity of MRSA to these antibacterials, clinicians should be cautious when treating patients with MRSA infections, particularly in

developing nations where there are limited resources for correctly identifying the different strains of MRSA. Being sensitive to antibiotics does not guarantee that MRSA will remain sensitive to them over time.

The other areas of concern regarding MRSA sensitivity to antimicrobials is knowledge of the different strains of MRSA and their breakpoints. “A breakpoint is a chosen concentration (mg/L) of an antibiotic which defines whether a species of bacteria is susceptible or resistant to the antibiotic” (British Society for Antimicrobial Chemotherapy (BSAC),2019).The breakpoints of antibacterials are vital in correct treatment. As stated by Turnidge and Paterson (2007),it is important to note the breakpoints of antibiotics, and their pharmacokinetics and pharmacodynamics, prior to them being used clinically. Breakpoints are used to define susceptibility and resistance to antimicrobials. Turnidge and Paterson (2007) added that it is the job of clinical laboratories to give that information to prescribers. The European Committee on Antimicrobial Susceptibility Testing [EUCAST] (2013) has defined the breakpoints for antimicrobials. Furthermore, clinical breakpoints are used in clinical microbiology laboratories to indicate to clinicians the quantity of a micro-organism which is known as the minimal inhibitory concentration (MIC) and whether that micro-organism is sensitive, intermediate or resistant to an antibacterial (Mouton et al., 2011).This information will guide clinicians in making their treatment plan.

## 2.7 Pathogenesis of hospital-acquired MRSA infections

There are five different stages in the pathogenesis of *Staphylococcus aureus* infections. Archer (1998, p. 1179) listed these five stages of pathogenesis as: (i) colonisation; (ii) location; (iii) systemic dissemination and /or sepsis; (iv) metastatic infection; and (v) toxinosis. Colonisation occurs when there is an infection or increase in the number of organisms at a site (Archer, 1998; Lowly, 1998).When the immune system is weakened, that allows for colonisation. For example, patients who are hospitalized for other underlying diseases are vulnerable to being colonised with *Staphylococcus aureus.* Diseases such as diabetes mellitus and HIV infection weaken the immune system and allow for colonisation of other organisms such as MRSA (Shorr, 2007).When there is an insertion of indwelling catheters or surgery, this may allow for bacteria to colonise the different sites too.

MRSA switches phenotypes depending on its location (I. M. Gould et al., 2012). Certain disease conditions enable MRSA to make these phenotypic changes, which are particularly favourable to persistent or chronic diseases like osteomyelitis and endocarditis (Gordon & Lowly, 2008; I. M. Gould et al., 2012).

After spreading through local sites, MRSA can then infect the blood which in turn causes sepsis. It can then spread to the peripheries and organs, causing septic shock. Dissemination occurs after sepsis. During dissemination, the organs of the body then become affected, causing further serious complications. There is high mortality associated with MRSA dissemination (Gordon & Lowly, 2008). The virulence factors possessed by MRSA enable it to disseminate and it is more pathogenic than any other organism (Archer, 1998; Crossley & Arthur, 1997). Lastly toxinosis occurs from systemic and local spread of MRSA. This causes toxins which in turn causes syndromes like scalded skin syndrome, toxic skin syndrome and food-borne gastroenteritis (Archer, 1998).

## 2.8 Epidemiology of MRSA

### 2.8.1 Global overview

The epidemiology of MRSA diseases, both healthcare-acquired and community-acquired, changes across different geographical and healthcare settings. A summary of the prevalence of MRSA across regions is shown in Table 1, below. Accurate information of the scope of MRSA is needed for prevention and control in different locations.

Table 1. *Prevalence of MRSA across regions.*

| Region | Prevalence of MRSA (%) |
|---|---|
| *Australasia* | |
| Australia | 10-40 |
| New Zealand | 10-30 |
| Papua New Guinea | No data on prevalence to date |
| *Other regions* | |
| Africa | 20-40 |
| America (North and South) | 20-40 |
| Europe | 20-30 |
| South-east Asia | 20-70 |

*Sources*: (Coombs et al., 2009)(Falagas et al., 2013); (Institute of Environmental Science and Research [IESR], 2012; Ministry of health, 2016);(Bouchiat et al., 2015; Moet et al., 2007).

The epidemiology of MRSA is changing (Chambers, 2001; Hryniewicz, 1999). It was believed by some scholars that the resurgence of MRSA was due to several reasons, namely: the overuse of antibiotics, a lack of proper infection control measures, and the increased resistance of MRSA strains to other classes of antibiotics by mutation (Hryniewicz, 1999). Other researchers included diseases such diabetes and HIV which have proven to be the factors that allowed for possible colonization of MRSA (Boucher & Corey, 2008; Chambers, 2001; Lowly, 1998). Yet others associated colonization with the two types of strains of MRSA (Roghmann, Siddiqui, Plaisance, & Standiford, 2001;Eko,Forshey ,Carrel,Schweizer,Perencevich & Smith,2015).

The global burden of MRSA incidence may be documented from prevalence and epidemiological studies of MRSA around the world. The epidemiology of HA-MRSA in the United Kingdom varies across the different countries (England, Northern Ireland, Scotland and Wales). It was increasing in the years before 2004; however, it was reduced due to continuous monitoring and surveillance and the preventative interventions that were implemented (Johnson, Pearson, & Duckworth, 2005).

Across North and South America, the highest prevalence rates (>50%) were reported In the United States (Mejia, Zurita, & Guzman-Blanco, 2010; Stefani et al., 2012).The trend is similar across the Asian continent (J. H. Song et al., 2011) where Japan had the highest prevalence rates of MRSA in all of Asia (Boyce et al., 2005). In contrast, the

situation was different in India and the Philippines, and the prevalence rates were lower for these countries (Grundmann et al., 2010).

The situation in Australia is quite different to the United Kingdom. A study conducted in the 1990s showed that after 20 years of trying to eradicate, HA-MRSA continued to increase and remained problematic in acute care institutions (McDonald, 1997). The reasons why MRSA remains problematic are; firstly, patients are at high risk of developing infections and secondly there are numerous entry points that allow MRSA to get into the body, for example people with burns, open wounds, feeding tubes, catheters and IVs all have open areas on their body where MRSA can enter (CDC,2017).However, after a further eight years the trend had changed significantly, and indicated variations across different Australian states(Boyce et al., 2005). Some states recorded high prevalence rates whilst others had varying rates. These results reflect the type of preventative measures that had been taken across Australia and whether they were effectively performed and maintained. New Zealand, however, has reported the highest rates of invasive and non-invasive *Staphylococcus aureus* infections among the developed nations (Williamson , Zhang, Ritchie, Fraser, & Baker, 2014).

There is little to no data on the epidemiology of MRSA in the Pacific region. Most developing countries lack systematic surveillance of MRSA to accurately record the prevalence. There is, however, data on the prevalence of MRSA among Pacific people living outside of the Pacific countries. Data on the prevalence of MRSA among Pacific peoples in New Zealand (Institute of Environmental Science and Research limited [IESR], 2008) shows it is generally high.

## 2.9 MRSA prevalence at different sites in hospital settings

MRSA is prevalent at different sites, in different age groups and in association with different diseases that patients present within a hospital setting. Some studies showed a high prevalence of MRSA in blood cultures from the special care nursery, medical and intensive care units (Coello, Glynn, Gaspar, Picazo, & Fereres, 1997; John, Naraqi, & McDonnel, 1990; World Health Organization, 2009b).Yet ,others reported that approximately 80% of MRSA isolates were from the intensive care units (Atilano, Pena, Chua, & Coronel, 2001; Hardy, Oppenheim, Gossain, Gao, & Hawkey, 2006). MRSA was

highly prevalent in post-operative wound infections (Coello et al., 1997).There were variations in prevalence rates from different sites including different disease states of the patients (Weber, Raasch, & Rutala, 1999). Mulligan et al. (1993) emphasized that the sites of colonisation of MRSA are very important and the frequency of pathogens vary by infection sites. The disease state of a patient may predict the prevalence of MRSA colonisation as well. Furthermore,Roghmann et al. (2001) emphasised that the risk of a patient of being colonised by MRSA is dependent on their clinical status. Again all these studies discussed that the trend for MRSA infection or colonisation depends on these factors; the different sites, age groups of patients and the disease state of patients.

## 2.10 Morbidity and mortality due to MRSA

There have been varying statistics reported on the deaths caused by MRSA. Eighty-seven percent of deaths associated with methicillin-resistant *Staphylococcus aureus* were reported in hospitals across England and Wales (Office for National Statistics (ONS), 2017). Across Asia, including India, there are still over fifty percent of deaths caused by MRSA in hospitals (Molton et al., 2013). Other studies have shown that *Staphylococcus* infections are the cause of considerable mortality and morbidity in the world, despite the development of antimicrobial agents (Beam & Buckley, 2006; Dilnessa & Bitew, 2016; Kejela & Bacha, 2013; Ortwine & Bhavan, 2018; Pai et al., 2010; Rajaduvaipandi et al., 2006). Furthermore, a study by Shurland, Zhan, Bradham, and Roghmann (2015) found that MRSA contributed to more deaths than Methicillin-Sensitive Staphylococcus aureus (MSSA).

The economic burden of healthcare-associated infections caused by multi-drug resistant organisms including MRSA is greater than the economic burden caused by other organisms that are not multi-drug resistant (National Nosocomial Infections Surveillance [NNIS], 2004; Stone, 2009). MRSA infections are associated with higher costs attributed to longer hospital stays, higher cost of treating patients with vancomycin and the cost of isolation procedures. In a study in the USA, the cost of treating a patient with HA-MRSA was found to be approximately twice as much as for patients with other infections (Yochay et al., 2005).Life threatening infections like sepsis (blood stream infection), endocarditis (inflammation of the endocardium) and osteomyelitis (bone infection) caused by MRSA have been reported from several parts

of the world, mainly in developing countries (Couto et al., 1995; Cox, Conquest, Mallaghan, & Marples, 1995; Hassoun et al., 2016). The prevalence of MRSA causing infections and deaths varies around the world (Hassoun et al., 2016). Papua New Guinea may share similar or have different trends when compared to other countries in terms of MRSA prevalence and epidemiology; however, due to the gaps in the literature, the prevailing situation in the country is unknown.

## 2.11 Antimicrobial susceptibility profile of MRSA

MRSA has become a therapeutic problem worldwide due to its resistant to penicillin-group of antibiotics. As discussed previously, this bacterium has developed resistance to beta-lactams by producing an enzyme called beta-lactamase (Shariq et al., 2017). Over the years MRSA has developed resistance to most antibiotics and therefore it has become very difficult to treat. To understand the emerging antibiotic-resistant trends of MRSA, a susceptibility profile study is required (Boucher & Corey, 2008). This is supported by World Health Organisation's aim to monitor antibiotic resistance globally (World Health Organization, 2014b). Such studies form the basis for the development of global strategies and infection control policies to reduce the spread of MRSA in healthcare settings. Moreover, a detailed knowledge of the susceptibility profile of MRSA will assist in the development of effective strategies to curb the wider growing problem of antibiotic resistance. In Europe an antibacterial surveillance has documented the use and consumption of antibiotics to standardise its use across hospitals for over 20 years (Ansari, Erntell, Goossens, & Davey, 2009). This type of surveillance will restrict unnecessary use of antibiotics by clinicians, thus reducing the risk of resistance.

Different hospitals in different countries use different antibiotic sensitivity guidelines. However, it has been reported across the globe that MRSA are clinically resistant to all beta-lactam antibiotics (Boyce et al., 2005; Knight et al., 2012; Sit et al., 2017). Despite the use of different guidelines, whether it be the European Union Committee on Antimicrobial Susceptibility Testing(EUCAST) or the Clinical and Laboratory Standards Institute(CLSI), MRSA is still resistant to all beta-lactams. The confirmatory discs used for diagnosis of MRSA in the past were either oxacillin or cefoxitin. However, it has been reported that oxacillin has proven to be less effective in the confirmation of MRSA than cefoxitin and many hospitals now use cefoxitin as a confirmatory disc to

confirm MRSA (Knight et al., 2012). Furthermore, the CLSI recommends cefoxitin (30 µg) to be used as a confirmatory disc for MRSA (Clinical and Laboratory Standards Institute [CLSI], 2013). Other methods of sensitivity testing by laboratories have also recommended cefoxitin to be more reliable than oxacillin for MRSA identification (Skov et al., 2014).

## 2.12 Preventative measures to reduce MRSA in healthcare settings

### 2.12.1 Hand hygiene

"The effectiveness of infection control practices varies significantly across different hospital settings"(Sadsad, Sintchenko, Mcdonnel, & Gilbert, 2013, p. 1).Healthcare workers and guardians of patients may reduce the spread of *Staphylococcus* infections by following good hand hygiene practices, for example the use of hand disinfectants or hand gels. Healthcare workers hands are the mode of transmission of healthcare associated pathogens including MRSA (Allegranzi & Pittet, 2009). There should, however, be a culture where patients and their relatives understand the practice of hand hygiene and its importance too. Hand hygiene has been proven to prevent the spread of infections in health care settings (Sadsad et al., 2013; World Health Organization, 2002, 2009a, 2009b).Pittet (2001)emphasised that effective infection control policies such as hand hygiene have helped reduce HAIs. Moreover, other studies have also shown that when hand hygiene policies were implemented, there was a decline in HA-MRSA (Barnes & Jinks, 2008; Marimuthu, Pittet, & Harbarth, 2014). By using effective hand hygiene procedures, the benefits are great: the cost of having to treat hospital acquired MRSA is reduced and money is saved; the chance of having MDROs are reduced; and longer hospital stays are avoided and patients do not get MRSA .

### 2.12.2 Contact precautions

The spread of MRSA may be reduced when healthcare practitioners have less contact with patients who are colonised with MRSA since it is believed to be spread by the hands of healthcare workers (Mcbryde, Bradley, Whitby, & McElwain, 2004).Healthcare workers should have on-going training and be judicious in their care of patients. Limiting the ratio of healthcare workers to the number of patients they

care for has contributed to the reduction in the spread of HA-MRSA (Sadsad et al., 2013).

Personnel protective equipment (PPE) must always be worn when attending to patients. This equipment includes gloves, and eye, hand and foot protection. When treating patients with MRSA infections health-care workers must be well protected so that they do not transmit infection onto other patients. After attending to each patient,PPEs,mainly gloves, must be changed. In a country such as Papua New Guinea, one factor that may have an impact on continuous provision of gloves is financial constraints. The second factor would be the ignorance of healthcare workers to change gloves after attending to each patient. However these challenges can be rectified. If there is continuous providence of PPEs from a set budget and continuous awareness, those factors mentioned above may can be minimised.

### 2.12.3 Antibiotic surveillance

Documenting an antibiotic profile of multi-resistant organisms is valuable in creating programmes to tackle the increasing prevalence rates of MDROs such as MRSA in hospital settings (Maragakis et al., 2014). In addition, the CDC recommends that understanding the burden of MRSA – that is, how much is occurring and where it is occurring – is essential in developing effective prevention programmes and measuring their impact (Centres for Disease Control and Prevention, 2010). To prevent the therapeutic challenge of MRSA, it is important to do continuous antimicrobial surveillance of MRSA in order to be able to formulate antibiotic policies and effective infection control policies. Avoiding unnecessary prescribing of antibiotics by clinicians will help prevent antimicrobial resistance.

A study has recommended the screening of all hospital patients for MRSA before admission which reduces the possibility of having HAIs transmitted in the event of an outbreak (Wernitz et al., 2005). Others, however, believe that this method still does not completely stop patients from acquiring MRSA whilst admitted (Harbarth, Fankhauser, & Schrenzel, 2008).

All in all, careful hand washing, use of standard infection control practices and accurate prescribing will be effective in moving towards the reduction of HA-MRSA (Coia, Duckworth, & Edwards, 2006).In addition, different infection control measures have

different impacts on the prevalence and incidence of MRSA across different ward specialities of healthcare settings (Sadsad et al., 2013).Therefore, infection control preventative measures have to be contextualised for greater effectiveness.

## 2.13 Infectious diseases in Papua New Guinea

Papua New Guinea is currently faced with resistance to antibiotics(World Health Organization, 2018). This antibiotic resistance includes bacterial resistance and disease resistance. Bacterial resistance to antibiotics includes organisms like *Klebsiella pneumoniae*, *Escherichia coli* and *Staphylococcus aureus*. "There are five main factors that give rise to antibiotic resistance: weak health systems, poor regulation and dispensing of antimicrobials, overuse and misuse of antimicrobials in the animal sector, lack of surveillance monitoring systems and low awareness"(World Health Organization, 2016).

The WHO's latest report on infectious disease resistance to drugs in Papua New Guinea includes TB,HIV, malaria and influenza (World Health Organization, 2016). MRSA was not included in the WHO report due to unavailability of data. These diseases have become resistant to commonly used drugs and the burden of the disease is putting a tremendous strain on the health department and the government of Papua New Guinea. Papua New Guinea has the largest epidemic of HIV in the Pacific region (Centres for Disease Control and Prevention [CDC], 2013a). The ten most common diseases causing death in Papua New Guinea, as reported by Centres for Disease Control and Prevention [CDC] (2013a)are: lower respiratory infection, cancer, diabetes, TB, ischaemic heart disease, chronic kidney disease, malaria, stroke, diarrhoeal disease and HIV.

The WHO, in collaboration with the CDC, has done a tremendous job worldwide to combat antibiotic resistance. Surveys are carried out worldwide, including Papua New Guinea for antimicrobial resistance by the WHO. The surveys and research focused primarily on antibacterial resistance. It is believed that determining the scope of the problem would enable effective strategies to curb this growing trend of antimicrobial resistance (World Health Organization, 2014a). With a good surveillance system in place, WHO can then collect and report accurately the prevalence of MRSA in a country such as Papua New Guinea.

## 2.14 Conclusion

As this literature review has shown, MRSA is a public health concern and its prevalence varies geographically. It causes fatal infections in hospitals and has a resistance mechanism that is terrifying. It becomes resistant to many antibiotics and thus demands proper surveillance and the monitoring of antibiotic use. MRSA spreads in hospitals mainly due to lack of infection control strategies.

Papua New Guinea is a developing country and may experience similar or worst-case scenarios when compared with other countries that have been discussed in this chapter. It is currently faced with antibiotic resistance as reported by World Health Organization (2014a). Therefore, a study of the prevalence and antimicrobial susceptibility pattern of MRSA in Papua New Guinea is timely and will be of great benefit.

# Chapter 3 Research Methodology

## 3.1 Introduction

This chapter presents the methodological framework employed in this study, including research aims, research design, data collection procedures, and statistical analysis used to analyse data. The ethical context of this study and its benefit to Port Moresby and Papua New Guinea are discussed. The limitations of this study are also presented and discussed.

## 3.2 Methodological framework

This research employed a positivist philosophical worldview and utilised an objectivist epistemology. An objectivist epistemology is independent of the subjects being studied (Kaya, 2013).The researcher does not have contact or association with the subjects and the findings are not influenced by the researcher. This project is an epidemiological study, in the records of the prevalence of MRSA over five years were observed. In an epidemiological study, the prevalence of diseases is studied to observe a pattern or trends over time (Pearce, 2012). Another definition of epidemiology by Inhorn (1995) describes it as “a statistical subdivision of biomedicine”(p.285).

A positivist worldview involves scientific methods, and the making of predictions and generalisations from the data collected. Cresswell (2014) stated that positivism is associated with scientific method and uses quantitative analysis and statistical techniques. In this research, data was collected and analysed using statistical techniques to interpret it and arrive at a conclusion. The observation and collection of data to arrive at a conclusion in this research can only be explained when a positivist worldview is adopted. Positivists assume that reality is objective and can be explained by what lies therein. In this study the statistical technique used for analysis was the chi-square test of independence. This analysis was used to show an association between MRSA and categorical variables of interest. It is deductive in nature whereby a large amount of data is gathered to explore and answer research questions, or confirm or reject hypotheses (Cresswell, 2014; Kaya, 2013).

### 3.2.1 Research aims

The main aim of this study is to document, report on and make significant associations in relation to the prevalence and susceptibility pattern of methicillin-resistant *Staphylococcus aureus* (MRSA) at the Port Moresby General Hospital, Papua New Guinea.

The research questions are as follows:

1. What is the prevalence of confirmed methicillin-resistant *Staphylococcus aureus* among *Staphylococcus aureus* isolates?
2. What is the antimicrobial susceptibility profile of methicillin-resistant *Staphylococcus aureus* isolated from all sites in Port Moresby General Hospital?

## 3.3 Research design

The design of this study was a retrospective cohort study. This study gathered data for a five-year period undertaken prospectively. The data acquired in this study are from records of patient's specimens, whereby the specimens were initially cultured and confirmed for MRSA using biochemical methods and sensitivity testing using the Kirby-Bauer disc diffusion method according to Clinical Laboratory Institute guidelines (Clinical Laboratory Standards Institute [CLSI], 2013; Pai et al., 2010). A cohort study falls under the category of observational quantitative studies (J. W. Song & Chung, 2011). It is an analytic study that examines aetiology and causal relationships. A cohort study has several advantages: it is safer and easier than a randomised controlled trial (RCT), a study that requires experiments to be conducted; it is used to produce risk factors of an outcome; and it is cheaper and less time consuming than other approaches(Mann, 2003). The disadvantages of a cohort study, as highlighted by Mann (2003) are:a cohort study does not gather in-depth data about people's experiences of phenomena; and confounding variables can be problematic, particularly in a prospective cohort study.

The current study is aimed at testing for associations between MRSA and a number of other variables of interest. As emphasised by Euser, Zoccali, Jager, and Dekker (2009) a cohort study does not always show a cause-and-effect relationship but can show interesting new associations that have not been hypothesised. In this study, secondary

data was collected from confirmed MRSA cases from the laboratory records for the years 2012 to 2016 at the Port Moresby General Hospital, Papua New Guinea. The data included all patients' records, from urban clinics, private clinics around Port Moresby, and also specimens sent from other provinces outside of the National Capital District. The MRSA isolates were from specimens such as pus swabs (ear swabs, nasal swabs, and eye swabs), catheter tips, sputum, blood, body fluids, urine, and cerebrospinal fluid(CSF) that were sent in for microbiology, culture and sensitivity testing for suspected *Staphylococcus* infection. This is similar other studies done elsewhere in the world (Pai et al., 2010; Rajaduvaipandi et al., 2006; Saikia, Nath, Choudhury, & Sakar, 2009; Tiwari et al., 2009).

## 3.4 Research setting

Port Moresby General Hospital is a referral and teaching hospital for the country. It is a level seven hospital, located in Korobosea, a suburb of the National Capital District, and is adjacent to the School of Medicine and Health Sciences of the University of Papua New Guinea. The hospital caters for patients in the National Capital District, Central Province and the other 20 provinces. Patients from urban clinics and provinces outside of National Capital District are referred to Port Moresby General Hospital regularly to receive specialised health services.


*Figure 2*: Port Moresby General Hospital.Source: (Wikipedia, n.d.-b)

Port Moresby General Hospital (see Figure 2) admits approximately 500 patients per month. It caters for 280,000 people who seek specialised health services. The hospital has approximately 5,000 beds and has specialised services and specialist medical officers for the country. It has the only microbiology laboratory in the country that performs complete microscopy, culture and sensitivity testing for all specimens. The

collection of data for this study took place in the clinical microbiology laboratory of the hospital.

## 3.5 Data

Data records were collected from the records of all in-patients and out-patients (infants to adults), including urban clinics around Port Moresby and, occasionally, clinics in other provinces beyond the National Capital District. These patients were either colonised or infected with MRSA in the five years, from 2012-2016.

## 3.6 Data collection

Data were obtained from daily logs books at the microbiology laboratory at Port Moresby General Hospital. A structured self-prepared Microsoft Excel spread sheet was developed for collection of the variables needed for the study. Prior to data collection, identifiable variables such as names of patients were coded , and other variables aggregated by the researcher. Data was then gathered from the log books kept at the microbiology laboratory at the hospital and entered into the spread sheet. The Excel files were organised in years and kept in two different laptops. A master copy was always copied onto a different computer at the end of each day of data collection.

## 3.7 Measures

The variables measured in this study were age, gender, wards, specimen types, patient's clinical diagnosis and the six different anti-staphylococcus agents used, based on the EUCAST and the CLSI. The anti-staphylococcus agents tested were chloramphenicol (30µg), septrin (25 µg), erythromycin (15 µg), tetracycline (30 µg),vancomycin (30µg) and cefoxitin (30 µg). These variables were coded, grouped and categorised to be made easier for data analysis (see Appendix D for the coding system). Previous studies used these variables to determine the prevalence of MRSA (Beam & Buckley, 2006; Dilnessa & Bitew, 2016; Kejela & Bacha, 2013; Pai et al., 2010).

## 3.8 Sample size

The sample size was initially calculated using previous studies' prevalence rates used internationally. As this study was a retrospective observational study, no one formula was suitable to calculate the sample size for this study(Daniel, 1999).

Previous studies suggested that the proposed study's prevalence rate of MRSA isolated from different sites was expected between 20-30% for a period of 12 months in healthcare settings (Beam & Buckley, 2006; Kejela & Bacha, 2013; Pourhoseingholi, Valedi, & Rahimzadeh, 2013). The sample size was calculated using Daniel's (1999) formula:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

where n=sample size; Z= a statistic corresponding to the level of confidence, and for 95% CI, the conventional Z value =1.96; P= the expected prevalence, which can be obtained from previous studies by other researchers; and d =the precision, corresponding to the effect size.

The estimated prevalence (P) was 30%, as shown by previous studies (Beam & Buckley, 2006; Kejela & Bacha, 2013; Wareng, Foster, & Daw, 2014). Daniel (1999) suggested estimated *p* value to be 0.05 for prevalence rates that are between 10% and 90%. The assumed effect size or precision (d) would be 0.01 at 95% confidence interval (Z=1.96).The estimated sample size (n), when calculated using the formula and the stated values for Z, P and d, was 1,825. Therefore, the total estimated confirmed cases of MRSA were 1,825.However, in this study a total of 1,006 confirmed MRSA samples were gathered for the five years 2012-2016.Since this was the first time a study was carried out in Papua New Guinea, different sample sizes can be proposed for further research in future after this study, considering other factors that might be involved in the variations of prevalence rates and the MRSA antimicrobial profile.

## 3.9 Procedures for confirming MRSA

MRSA was isolated using MacConkey agar, blood agar and chocolate agar and incubated for 24 hours in a 37˚C incubator, from specimens such as pus swabs (ear, nose and eye, cervical and wound), catheter tips, sputum, blood, body fluids, urine and CSF by the diagnostic laboratory. These specimens were sent in for routine or suspected *Staphylococcus* infection for microbiology, culture and sensitivity testing. Morphological and biochemical testing were performed to confirm *Staphylococcus aureus*. Sensitivity testing was performed using the Kirby-Bauer disc diffusion method on Mueller Hinton Agar (MHA). The sensitivity and confirmation of MRSA were

compared against the EUCAST and the CLSI guidelines. The panel of antibacterials comprised: chloramphenicol (30 µg), erythromycin (15 µg), septrin (25 µg), tetracycline (30 µg) and vancomycin (30 µg). MRSA was confirmed using the diagnostic disc cefoxitin (30µg) and oxacillin (1 µg). A disc zone size of less than 22 mm was confirmatory of MRSA (Clinical and Laboratory Standards Institute [CLSI], 2013).The CLSI 2010 and 2013 antimicrobial susceptibility testing guidelines were used. Standard recommended zone sizes were used to determine sensitivity or resistance to the other antibacterials. A report was then sent out to clinicians with the full antimicrobial profile of the MRSA for them to treat accordingly.

## 3.10 Statistical analysis

The data were entered into Microsoft Excel prior to analysis. They were then imported from Excel into Statistical Package for Social Science (SPSS) version 25 (Pallant, 2010) and coded for analysis (see Appendix C). Firstly, the descriptive statistics for all variables were computed using SPSS and Excel to document the frequency of MRSA amongst the variables. This answered the first aim of this study, which was to document the prevalence of MRSA at Port Moresby General Hospital.

The chi-square statistical test of independence technique was chosen to explore the association between categorical variables. The sensitivity pattern of MRSA was analysed against categorical variables to confirm if they had any significant association with the five anti-staphylococcal tested according to CLSI and EUCAST guidelines. The statistical technique chosen and used was the chi-square test of independence. Using this statistical treatment gave an indication of the sensitivity pattern of MRSA as well.

For the analysis, $p \leq .05$ was considered to indicate statistical significance. This enabled this study to document the sensitivity pattern of MRSA based on the association with the variables of interest. The nature of the data gathered can only allow the chi-square test of independence to be used. The second question of this research was answered using this test.

## 3.11 Ethical considerations and approval

Ethics approval (18/112) was obtained from the Auckland University of Technology Ethics Committee (AUTEC) on March 19,2018 (see Appendix A). Permission for

collection of desensitized data was sought from Port Moresby General Hospital in Papua New Guinea, the study site, using the approved research proposal (PGR1) from the Faculty of Health and Environmental Sciences, Auckland University of Technology. Permission was granted for data collection on March 26,2018. Data collection commenced on April 9,2018 and ended on June 15,2018.

## 3.12 Confidentiality and anonymity

Patients' confidentiality and anonymity were protected by coding identifiable information (see Appendices C and D).The patients' identifiable information, such as names, were aggregated, decoded and always kept protected by the researcher during the time of data collection. The other variables were also aggregated. This ensured total anonymity. The patients were not required to give consent; however, the hospital, the custodian of their information, gave permission on their behalf with the condition that the information taken was to be kept confidential. Data was saved in two different locations in a password protected file at the end of each day whilst data collection proceeded, to ensure back up if the data on one computer was lost or destroyed. A master copy was always kept for the five years' data. The researcher the primary supervisor and the secondary supervisors were the only people who had access to the data after completion of data collection.

## 3.13 Privacy

Secondary data was collected; however, patients' information was kept secure. The data was initially taken for diagnosis purpose and not intended for research, therefore a sensitive data management protocol was created to keep sensitive information privately stored and safe (see Appendix D for this protocol).

## 3.14 Beneficence

The findings of this study were intended to be beneficial for the hospital, the community and the country. This study will enable the hospital to create an effective infection control policy to curb healthcare associated infections caused by MRSA. The results from this study will also reduce the unnecessary use of antibiotics, reduce HAIs and create an infection control policy. Similar studies have been shown to reduce the unnecessary use of antibiotics and create effective infection control policies (Beam & Buckley, 2006; Dilnessa & Bitew, 2016; Kejela & Bacha, 2013; Pai et al., 2010;

Rajaduvaipandi et al., 2006). For the wider community, the benefit will be the reduction of antibiotic resistance.

The results from this study will be presented to the clinicians in the hospital and they may then come up with a standard treatment guideline for MRSA,which will assist in the reduction of the risk of this organism becoming multi-drug resistant. An infection control policy will also create a learning culture for guardians and relatives who come to the hospital to visit patients. This will benefit the community by educating them of the importance of reducing HAIs by, for example, the usage of hand wash or hand gels. For the country as a whole, the standard treatment guideline that is created by clinicians based on the findings of this study can be circulated to other provinces in Papua New Guinea for the treatment of MRSA infections and can be kept as a national policy with the Department of Health in Papua New Guinea.

## 3.15 Limitations of the study

The major limitations encountered in this study were: inconsistency or missing details in the results entered in the log books, and missing anti-staphylococcal agents, which meant that the panel of anti-staphylococcals tested was not complete. However, these limitations account for a small percentage (<2%) of the data and did not significantly affect the outcome of this study. Despite these limitations, the antimicrobial susceptibility pattern prevalence of MRSA was still determined and justified using previous literature. This is a first-time study for Papua New Guinea and may be considered an exploratory one, and the shortcomings may be addressed in future research.

# Chapter 4 Results

## 4.1 Introduction

This chapter presents the findings of this study in relation to the two research questions. Firstly, this chapter will present the prevalence of MRSA at Port Moresby General Hospital, Papua New Guinea. Secondly, it will document the antimicrobial susceptibility pattern of MRSA. As described in Chapter 3, original data was collected and entered into Microsoft Excel initially and then imported into the Statistical Program for Social Science(SPSS) for analysis. The general frequency and distribution of all variables are presented using SPSS descriptive statistics and Excel in tables and graphs in this chapter. Descriptive statistics are used to summarise and report the data. Percentages and frequencies are used to represent categorical variables. The chi-square test of independence is used to show association between MRSA and categorical variables.

## 4.2 Descriptive information of study variables

A total of 57,959 specimens (pus swabs, catheter tips, venous blood, sputum, aspirates, urine, cerebral spinal fluid, scrapings) for microscopy, culture and sensitivity (MCS) were received from 2012 to 2016.Of the total specimens received,1,098 were MSSA and 1,006 isolates were MRSA. All MRSA were tested against six antibacterials (chloramphenicol, erythromycin, septrin, tetracycline, vancomycin and cefoxitin/oxacillin) according to the EUCAST and the CLSI standards of antimicrobial susceptibility testing (Clinical Laboratory Standards Institute [CLSI], 2013; European Committee on Antimicrobial Susceptibility Testing [EUCAST], 2013).

Simple descriptive summary statistics was computed to answer research question one, which was to document the prevalence of MRSA among all variables used. Excel was used to analyse, tabulate and create graphs for some variables. The chi-square test of independence was used to determine significant association between categorical variables and the five antibacterials (erythromycin, chloramphenicol, septrin, tetracycline and vancomycin). The chi-square test of independence was also used to determine the susceptibility pattern of MRSA.

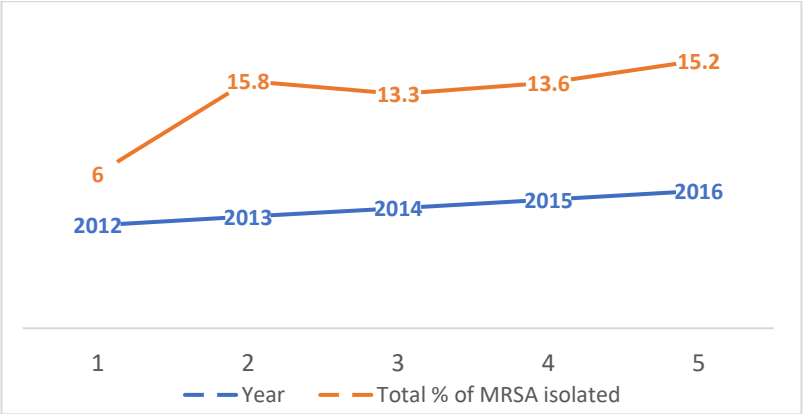


*Figure 3:*Prevalence of MRSA from 2012-2016. 1=2012, 2=2013, 3=2014, 4=2015, 5=2016.

The prevalence of MRSA over the five years of the study is shown in Figure 3. The total prevalence of MRSA isolated from all specimen (blood,pus swabs, body fluids, urine)in the five years was 63.9%. The lowest prevalence of MRSA from all specimen was recorded in 2012(6%). The highest prevalence was recorded in 2013 (15.8%). There was an increase in 2013 (15.8%). The prevalence of MRSA dropped in 2014 (13.3%), however increased again in 2015 (13.6%) to 2016 (15.2%). The most likely explanation for the increases would be lack of infection control measures both on the wards and at the laboratory. There is most likely cross-contamination issues in the laboratory.

Table 2. *Distribution of MRSA by gender.*

| **Gender** | **Frequency** | **Percentage** | **Cumulative Percentage** |
|---|---|---|---|
| Female | 474 | 47.1 | 47.1 |
| Male | 529 | 52.6 | 99.7 |
| No sex recorded | 3 | 0.3 | 100.0 |
| Total | 1006 | 100.0 | |

Table 2 represents the prevalence of MRSA across the gender of patients. MRSA positivity among females was slightly higher than in males. A total of 0.3 percent of patients had their gender missing from the records.

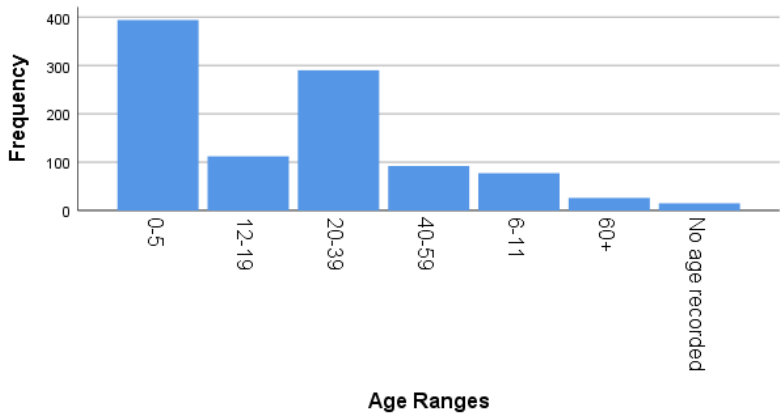


*Figure 4*: Frequency distribution of MRSA by age groups. Data for 60+ includes both the 61-70 and 70+ age groups.

The prevalence of MRSA among different age groups is presented in Figure 4, above. The highest frequency of MRSA was isolated from the 0-5 years age group (39.2%), followed by the 20-39 years age group (28.8%) and the 12-19 years age group (11.1%).The 0-5 years of age group are those that are more susceptible to infections thus the high frequency. The lowest prevalence of MRSA for a group of known age was observed in patients greater than 60 years of age (2.6%);however, the patients with "no age recorded" were observed to have the lowest MRSA prevalence of all, at 1.5 %.

Table 3. *Frequency distribution of MRSA by clinical specimen.*

| Specimen | Frequency | Percentage | Valid Percentage | Cumulative Percentage |
|---|---|---|---|---|
| Aspirate | 46 | 4.6 | 4.6 | 4.6 |
| Bone | 2 | 0.2 | 0.2 | 4.8 |
| Catheter tip | 13 | 1.3 | 1.3 | 6.1 |
| CSF | 2 | 0.2 | 0.2 | 6.3 |
| Scraping | 1 | 0.1 | 0.1 | 6.4 |
| Sputum | 41 | 4.1 | 4.1 | 10.5 |
| Swab | 738 | 73.4 | 73.4 | 83.9 |
| Urine | 29 | 2.9 | 2.9 | 86.8 |
| Vb | 134 | 13.3 | 13.3 | 100 |
| Total | 1006 | | | |

*Note*: CSF= cerebral spinal fluid, Vb = venous blood.

The prevalence of MRSA among the different clinical specimens is shown in Table 3.MRSA was isolated in nine clinical specimens. The prevalence of MRSA was significantly different among the different clinical specimen types. MRSA isolation was predominant in swab samples (73.4%), followed by venous blood (13.3%) and aspirates

(4.6%). The lowest isolation of MRSA was from the CSF (0.2%), bone (0.2%) and scrapings (0.1%)specimens. Over the five years, a smaller number of bone and scrapings specimen were received, thus a low prevalence was observed.

Table 4. *Distribution of MRSA by months (%).*

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2012** | 0.3 | 0.4 | 0.4 | 0.5 | 0.4 | 1.0 | 0.3 | 1.0 | 0.6 | 0.8 | 1.2 | 0.3 |
| **2013** | 1.3 | 1.1 | 0.9 | 2.1 | 2.7 | 1.9 | 2.3 | 1.9 | 2.8 | 1.3 | 1.3 | 0.7 |
| **2014** | 2.9 | 2.4 | 0.4 | 1.9 | 1.6 | 2.9 | 1.9 | 2.8 | 1.7 | 1.2 | 1.9 | 1.3 |
| **2015** | 1.9 | 1.0 | 1.8 | 2.1 | 1.0 | 2.4 | 2.2 | 0.9 | 1.8 | 2.0 | 3.4 | 2.5 |
| **2016** | 1.4 | 1.9 | 1.8 | 4.0 | 2.9 | 1.8 | 2.3 | 2.5 | 2.8 | 2.7 | 1.3 | 0.8 |

As presented in Table 4, it was found that MRSA prevalence increased slightly for all years in the months from December to March. However closer inspection of the table shows variations in some years. In the month of December, there was a decrease in the year 2016.There was a decrease in the month of December for the year 2012 also. For the months of January and February, the decrease was observed in years 2015 and 2016.For the month of March, a different trend was observed which saw an increase of MRSA in 2013 (0.9 %), a decrease in 2014 (0.4%), an increased again in 2015 to 1.8 % and the figure remained at 1.8 % in 2016. In the dry season, from June to September saw increases in the prevalence of MRSA in the years 2012 to 2014.However closer inspection of the table saw a decrease in MRSA for the years 2015 and 2016.In the month of October,MRSA prevalence increased from 2012 to 2013 (0.8% to 1.3%), and in 2014 it decreased to 1.2% and then increased again slightly in 2015 (2.0%) and 2016 (2.7%). In the month of November,MRSA prevalence increased from 2013 to 2015 (1.2%,1.3%,1.9%,3.4%); however, the figure decreased in 2016 to 1.3%.

Table 5. *Source of Staphylococcus aureus isolates in various clinical samples (2012-2016).*

| **Clinical sample** | **MSSA** | | **MRSA** | |
|---|---|---|---|---|
| | ***n*** | ***%*** | ***N*** | ***%*** |
| Aspirates | 16 | 3.4 | 42 | 9.4 |
| Blood | 99 | 2.5 | 129 | 1.5 |
| CSF | – | – | 2 | 0.2 |
| Pus | 886 | 52.3 | 769 | 47.2 |
| Sputum | 25 | 2.4 | 33 | 3.6 |
| Throat swab | 1 | 20.0 | – | – |
| Urine | 71 | 1.9 | 29 | 0.8 |

*Note*: MSSA = Methicillin-sensitive *Staphylococcus aureus*; MRSA = Methicillin-resistant *Staphylococcus aureus*; CSF = cerebral spinal fluid.

Of the total number of specimens (*n=57,959*) received in the five years (2012-2016), the highest prevalence of both MSSA and MRSA were observed in the pus specimens (see Table 5). However, MSSA (*n=886, %=52.3*) prevalence was higher than MRSA (*n=769, %=47.2*). The second highest prevalence of MRSA was from the blood specimens, (*n=121, %=105*), this prevalence of MRSA being higher than for MSSA in blood specimens (*n=99, %=2.5*). A total of 134 blood specimens received, mainly from paediatric wards and the special care nursery. The CSF and throat swab specimen are normally sterile specimens, hence the low prevalence of both MSSA and MRSA. The urine specimens were isolated with a higher prevalence of MSSA (*n=71, %=9.1*) than MRSA (*n=29, %=.8*). The aspirates were isolated with a higher prevalence of MRSA (*n=42, %=9.4*) than MSSA (*n=16, %=3.4*). Pleural aspirates (*n= 20, %=2.0)* accounted for most of the aspirates (hip, thigh, knee, tibia, tracheal and pericardial) that were received for microbiology, culture and sensitivity testing in the five years studied. MRSA is mainly favourable to lung infections, therefore the high prevalence observed in pleural aspirates.

Table 6. *Frequency of MRSA isolated from clinical samples per year.*

| **Specimen** | **2012 (%)** | **2013 (%)** | **2014 (%)** | **2015 (%)** | **2016 (%)** |
|---|---|---|---|---|---|
| Aspirates | 1.5 | 2.8 | 2.4 | 1.6 | 1.1 |
| CSF | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 |
| Pus | 3.7 | 3.7 | 9.2 | 10.6 | 12.5 |
| Sputum | 3.0 | 0.8 | 0.6 | 0.8 | 0.8 |
| Throat swab | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Urine | 0.1 | 0.3 | 0.2 | 0.1 | 0.1 |

There are significant variations in the trend of the prevalence of MRSA from different clinical specimens as observed in the five years studied(see Table 6). For the pus (wound swabs, abscess swabs, urethral swabs, ear, eye, nose swabs, catheter tips) specimens alone, the prevalence of MRSA increased from 9.2% in 2014 to 10.6% in 2015 and to 12.5% in 2016. The possible explanation for this increase would be related to the increase in pus swabs from wound infections. Wound infections increased in the years 2014-2016, contributing to the increase in the number of pus specimens. Of all pus swabs received, a total of 82 (8.2%) examples of MRSA isolated were from wound

infections. The highest prevalence of MRSA from pus specimens was from abscesses (17.7%), followed by pus swabs from wound infections (8.2%). The prevalence of MRSA from blood specimens increased in the years 2012 to 2014. The prevalence of MRSA from blood specimens saw a decrease in 2015.This decrease happened concurrently with the introduction of a BACTEC (Bacton Dickinson automated blood culture machine). The CSF and throat swabs produced less than 1% of MRSA isolated in all the five years. For the sputum specimens, the prevalence of MRSA decreased from 2012 (30%) to 2013 (0.8%),decreased further in 2014 (0.6%) and remained consistent in the years 2015 and 2016 (0.8%). For the urine specimens, the prevalence of MRSA increased from 2012 (0.1%) to 2013 (0.3%) and decreased in the year 2014 and remained consistent at 0.1% in 2015 and 2016. MRSA isolates from CSF only increased in 2013 (0.1%) and 2014 (0.1%). All throat specimens received had 0% MRSA isolated. The prevalence of MRSA in body fluids increased in 2013, however decreased from 2014 to 2016 (from 2.4% to 1.1%).

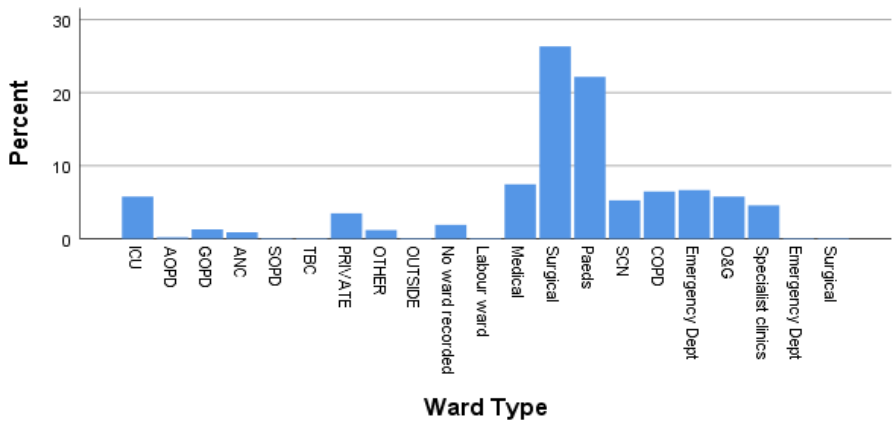


*Figure 5*: Frequency distribution of MRSA by wards.

AOPD=Adult out-patient department; O&G=Obstetrics & Gynaecology; COPD=Children's Outpatient Department; SCN=Special Care Nursery; TBC =Tuberculosis Clinic; SOPD=Surgical Outpatient Department;ANC=Antenatal Clinic; GOPD=Gynaecology Outpatient Department;ICU=Intensive Care Unit; Paeds=Paediatric wards; Outside=Mt.Hagen Hospital; Other=Pathology,X-ray,School of Medicine and Health Sciences, PNG Defence Force Clinic, urban clinics.

As observed in Figure 5, the highest rate of isolation of MRSA was from the surgical wards (26.7%), followed by paediatric wards (22.3%). The medical ward, emergency department, COPD and SCN had prevalences of 7.5%,6.7%, 6.5% and 5.3% respectively. This high prevalence on the surgical wards would be related to the increasing numbers

of wound swabs (8.2%) that were received from these wards. The lowest percentages of MRSA isolates were from the TB Clinic (0.1%) and the labour ward (0.1%).

Table 7. *Distribution of MRSA from in-patients (IP) and out-patients (OP).*

| Frequency | Percentage | Valid Percentage | Cumulative Percentage | |
|---|---|---|---|---|
| IP | 745 | 74.1 | 74.1 | 74.1 |
| No ward recorded | 17 | 1.7 | 1.7 | 75.7 |
| OP | 244 | 24.3 | 24.3 | 100.0 |
| Total | 1006 | | | |

The prevalence of MRSA among the categorical variables in-patients and out-patients is presented in Table 7. The prevalence of MRSA among in-patients was 74.1% whilst out-patients had a prevalence of 24.3%. Those patients with no ward recorded showed a prevalence of 1.7%. The out-patient data were gathered from the wards that admitted out-patients.

Table 8. *Frequency distribution of MRSA by clinical infections.*

| Clinical infections | Frequency | Percentage | Valid Percentage | Cumulative Percentage |
|---|---|---|---|---|
| Blood | 132 | 13.1 | 13.1 | 13.1 |
| Bone | 48 | 4.8 | 4.8 | 17.9 |
| CNS | 11 | 1.1 | 1.1 | 19.0 |
| CDM | 180 | 17.9 | 17.9 | 36.9 |
| DM | 34 | 3.4 | 3.4 | 40.3 |
| Joint infections | 8 | 0.8 | 0.8 | 41.1 |
| Others | 44 | 4.4 | 4.4 | 45.4 |
| RSD | 69 | 6.9 | 6.9 | 52.3 |
| Skin infections | 459 | 45.6 | 45.6 | 97.9 |
| UTI | 21 | 2.1 | 2.1 | 100.0 |
| Total | 1006 | | | |

*Note*: CNS=Central nervous system; CDM=Clinical details missing; DM= diabetes mellitus; RSD=respiratory system disorder; UTI =urinary tract infections; Others=cancer, endocarditis, pyomyositis.

Table 8 shows that the highest frequency and rate of isolation of MRSA was from skin infections (*n=459, %=45.6*), followed by blood infections (*n=132, %=13.1*) and respiratory disorders (*n=69, %=6.9*) respectively (see Table 8). Following these were bone infections (*n=48, %=4.8*), others (*n=44, %=4.4*), diabetes mellitus (n=34, %=3.4), and urinary tract infections (*n=21,%=2.1*). Of the total specimens received, 17.9% of

MRSA was isolated from patients whose clinical details were missing. The clinical diagnoses with the least prevalence of MRSA were from central nervous system infections (*n=11, %=1.1*) and joint infections (*n=8, %=0.8*).

Table 9. *Distribution of antimicrobial susceptibility pattern of MRSA.*

| **Antimicrobial agent** | **Sensitive** | | **Resistant** | | **Not tested** | |
|---|---|---|---|---|---|---|
| *n* | *%n* | *%n* | *%* | | | |
| Chloramphenicol (30µg) | 792 | 78.7 | 207 | 20.6 | 7 | 0.7 |
| Erythromycin (15 µg) | 680 | 67.6 | 273 | 27.1 | 53 | 5.3 |
| Septrin (25µg) | 608 | 60.4 | 62 | 6.2 | 336 | 33.4 |
| Tetracycline (30µg) | 931 | 92.5 | 63 | 6.3 | 12 | 1.2 |
| Vancomycin (30µg) | 962 | 95.6 | 39 | 3.9 | 5 | 0.5 |

Table 9 presents antimicrobial susceptibility distribution of MRSA. MRSA isolates were predominantly sensitive to vancomycin (95.6%) and tetracycline (92.5%).Higher resistance to erythromycin (27.1%) and chloramphenicol (20.6 %) by MRSA were observed (see Table 9). Overall, MRSA showed greater than 50% prevalence among all other organisms that were isolated in the years 2012-2016. The sensitivity among different specimens, age groups and wards may indicate a different antimicrobial susceptibility trend.

Table 10. *Sensitivity pattern of MRSA from out-patient wards.*

| **Out-patient** | **Sensitive (%)** | **Resistant (%)** | **Not tested (%)** |
|---|---|---|---|
| Chloramphenicol (30µg) | 78.0 | 21.5 | 0.4 |
| Erythromycin (15 µg) | 69.5 | 23.2 | 7.3 |
| Septrin (25µg) | 61.0 | 6.4 | 32.2 |
| Tetracycline (30µg) | 89.3 | 9.0 | 1.7 |
| Vancomycin (30µg) | 96.0 | 3.4 | 0.4 |

Table 11. *Sensitivity pattern of in-patient wards.*

| **In-patient** | **Sensitive (%)** | **Resistant (%)** | **Not tested (%)** |
|---|---|---|---|
| Chloramphenicol (30µg) | 78.0 | 20.3 | 0.79 |
| Erythromycin (15 µg) | 64.0 | 31.3 | 4.6 |
| Septrin (25µg) | 62.0 | 6.5 | 32.0 |
| Tetracycline (30µg) | 93.0 | 5.9 | 1.1 |
| Vancomycin (30µg) | 95.0 | 4.2 | 0.53 |

Table 10 and Table 11 show the sensitivity patterns of out-patient and in-patient wards. Both out-patients and in-patients showed higher sensitivities to vancomycin

(OP=96%,IP=95%) and tetracycline (OP=89.3%,IP=93%) whilst higher resistance was observed in erythromycin (OP=23%,IP=31%) and chloramphenicol (OP=21.5%,IP=20.3%).

Table 12. *Distribution of clinical infections and their sensitivity patterns (%).*

| **Clinical infections** | **CS** | **CR** | **CNT** | **ES** | **ER** | **ENT** | **VAS** | **VAR** | **VANT** |
|---|---|---|---|---|---|---|---|---|---|
| Blood | 9 | 2 | 0.1 | 9 | 4 | 0.6 | 7 | 1 | 5 |
| Bone | 4 | 1 | 0 | 3 | 1 | 0.5 | 2 | 0.2 | 2 |
| CNS | 1 | 0 | 0 | 1 | 0.4 | 0 | 0.4 | 0 | 0.5 |
| CDM | 15 | 3 | 0.1 | 13 | 5 | 6 | 0.1 | 13 | 1 |
| DM | 3 | 0.5 | 0 | 3 | 0.6 | 0.2 | 2 | 0.1 | 1.2 |
| Joint infections | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 |
| Others | 3 | 1 | 0 | 2 | 2 | 0.3 | 3 | 0.5 | 1 |
| Respiratory | 5 | 2 | 0.2 | 5 | 2 | 0 | 3 | 0.6 | 3 |
| Skin | 36 | 10 | 0.3 | 30 | 12 | 3 | 28 | 2 | 16 |
| UTI | 2 | 0.5 | 0 | 1.5 | 0.6 | 0 | 0.4 | 0.3 | 1 |

| **Clinical infections** | **SXTS** | **SXTR** | **SXTNT** | **TES** | **TER** | **TENT** |
|---|---|---|---|---|---|---|
| Blood | 13 | 0.4 | 0 | 12 | 0.7 | 0 |
| Bone | 0.3 | 5 | 0 | 5 | 0.2 | 0 |
| CDM | 3 | 17 | 1 | 17 | 0.1 | 0.2 |
| CNS | 1 | 0 | 0.10 | 0.10 | 0 | 0 |
| DM | 3 | 0 | 0 | 3 | 0.01 | 0 |
| Joint infections | 1 | 0 | 0 | 1 | 0 | 0 |
| Others | 4 | 0.6 | 0 | 4 | 0.7 | 0 |
| Respiratory | 7 | 0.1 | 0.1 | 7 | 0.3 | 0 |
| Skin | 44 | 2 | 0.3 | 42 | 3 | 0.5 |
| Urine | 2 | 0.2 | 0 | 2 | 0.4 | 0 |

*Note*: CNS = central nervous system infections; UTI = urinary tract infections; DM = diabetes mellitus; CDM = clinical details missing; Others = cancer, endocarditis, pyomyositis; CS = Chloramphenicol sensitive; CR=Chloramphenicol resistant; CNT=Chloramphenicol not tested; ER = Erythromycin resistant; ENT = Erythromycin not tested; SXTS = Septrin sensitive; SXTR = Septrin resistant; SXTNT = Septrin not tested; TES = Tetracycline sensitive; TER = Tetracycline resistant; TENT = Tetracycline not tested.

There were nine categories of clinical infections that were analysed against the five antibacterials for their sensitivities (see Table 12). These clinical infections had uniform sensitivity patterns and were all highly sensitive to septrin: skin infections (43.6%),blood(12.5%),respiratory disorders (6.7%), UTI (1.9%) and clinical details missing (17.2%).Higher resistance was observed towards erythromycin for the following clinical details: skin infections (12.3%),blood infections (3.5%), others (1.9%), and clinical details missing (4.6%).The clinical infections grouped under 'other'showed varying sensitivity patterns. CNS infections showed high sensitivity to the following antibacterials: chloramphenicol (1.0%), erythromycin (1.0%) and septrin (1.0%) whilst joint infections showed high sensitivities to chloramphenicol (0.8%), erythromycin (0.8%), vancomycin (0.8%) and tetracycline (0.8%). Closer inspection of the table shows that all clinical infections were highly sensitive to septrin, vancomycin and tetracycline.

Table 13. *Distribution of diagnostic antimicrobial discs for MRSA confirmation.*

| **Cefoxitin (30µg)** | | **Oxacillin (1µg)** | |
|---|---|---|---|
| *n* | *% n* | *%* | |
| 822 | 81 | 184 | 18 |

As shown in Table 13, the diagnostic discs used to confirm identification of MRSA using CLSI and EUCAST standards were the discs cefoxitin and oxacillin. A total of 81% of MRSA were confirmed with cefoxitin (30µg) whilst 18 % was confirmed with oxacillin (1µg).

## 4.3 Chi-square test of independence

The chi-square test of independence is used to explore relationships between two categorical variables (Pallant, 2010). For this analysis, age groups and gender were analysed using the chi-square test of independence against the panel of antibacterials to ascertain whether their association were significant or not. The statistical significance threshold was set at $p \leq 0.05$. This analysis was computed to answer research question 2, which was to document the susceptibility profile of MRSA.

Table 14. Crosstabulation of gender vs. antibacterial

| | Patients' gender | | | |
|---|---|---|---|---|
| Agents, n (%) | Female | Male | $\chi^2$ | *p*-value |
| Chloramphenicol | | | 4.594 | **.032** |

| | | | | |
|---|---|---|---|---|
| Sensitive | 391 (49.3) | 402 (50.7) | | |
| Resistant | 83 (40.9) | 120 (59.1) | | |
| Erythromycin | | | 3.499 | .061 |
| Sensitive | 335 (49.6) | 341 (50.4) | | |
| Resistant | 117 (42.9) | 156 (57.1) | | |
| Septrin | | | 5.678 | **.017** |
| Sensitive | 21 (33.9) | 41 (66.1) | | |
| Resistant | 300 (49.8) | 303 (50.2) | | |
| Vancomycin | | | .229 | .632 |
| Sensitive | 455 (47.5) | 503 (52.5) | | |
| Resistant | 17 (43.6) | 22 (56.4) | | |
| Tetracycline | | | .792 | .374 |
| Sensitive | 443 (47.6) | 488 (52.4) | | |
| Resistant | 25 (41.7) | 35 (58.3) | | |

Note. Significant *p*-value in **bold**.

A chi-square test for independence between gender and all five antibacterial (chloramphenicol, erythromycin, septrin, tetracycline, vancomycin), indicated a significant association only with chloramphenicol (30µg), $p<.05$ (see Table 14). The Chloramphenicol-resistant and Septrin-resistant group had a higher percentage of men (p=.032, p=.017, respectively).

Table 15. Crosstabulation of age vs antibacterial

| | Patients' age | | | |
|---|---|---|---|---|
| Agents, n (%) | 0-20 years | 21+ years | $\chi^2$ | *p*-value |
| Chloramphenicol | | | .721 | .396 |
| Sensitive | 412 (56.6) | 316 (43.4) | | |
| Resistant | 101 (53.2) | 89 (46.8) | | |
| Erythromycin | | | .665 | .415 |
| Sensitive | 341 (54.9) | 280 (45.1) | | |
| Resistant | 146 (57.9) | 106 (42.1) | | |
| Septrin | | | 4.338 | **.037** |
| Sensitive | 38 (66.7) | 19 (33.3) | | |
| Resistant | 284 (52.2) | 260 (47.8) | | |
| Vancomycin | | | .328 | .567 |
| Sensitive | 495 (56.1) | 387 (43.9) | | |
| Resistant | 19 (51.4) | 18 (48.6) | | |
| Tetracycline | | | 1.267 | .260 |
| Sensitive | 481 (56.0) | 378 (44.0) | | |
| Resistant | 26 (48.1) | 28 (51.9) | | |

Note. Significant *p*-value in **bold**.

A chi-square test for independence between age groups and all five antibacterial (chloramphenicol, erythromycin, septrin, tetracycline, vancomycin), indicated that

Septrin-resistant group had a higher percentage of men were 0-20 years (p=.037) than patients who aged over 21 years old.

# Chapter 5 Discussion and Conclusion

## 5.1 Introduction

This chapter summarises, compares, contrasts and critiques the findings in the context of the relevant literature to answer the two research questions which were concerned with the documentation of the prevalence of MRSA at the Port Moresby General Hospital and the antimicrobial susceptibility patterns of MRSA. The discussion has two relevant sections: the prevalence of MRSA and the sensitivity pattern of MRSA. In the conclusion section, a summary of the whole thesis, the strengths, the limitations of and recommendations of this study will be discussed.

## 5.2 Summary of relevant findings

### 5.2.1 Prevalence of MRSA

The prevalence of MRSA differs geographically around the world. There is scant literature on the prevalence of MRSA in the Pacific region, including Papua New Guinea. This study sought to determine the prevalence of MRSA in Port Moresby General hospital, Papua New Guinea. This is the first study in Papua New Guinea to report the prevalence of hospital-acquired MRSA. As mentioned in the literature review, MRSA is a major global health concern as it causes longer hospital stays, mortality and morbidity due to its resistance to higher category antibiotics. MRSA has caused HAIs in hospitals worldwide (Hassoun et al., 2016; Hussain, Shams, Ahmad, Perveen, & Riaz, 2005; Maragakis et al., 2014; Nickerson et al., 2009).

The prevalence of MRSA in this study was 63.9% (see Figure 3).This is consistent with studies in India that recorded prevalences greater than 50% (Anupurba et al., 2003; Bouchiat et al., 2015; Mehta et al., 1998; Tiwari et al., 2009).In a multi-national surveillance programme in Asia,Chen and Huang (2014) reported prevalences of hospital-acquired MRSA ranging from 30%-70%.The countries studies were: the Philippines with a prevalence of 38.1%; Thailand, 57%; and Vietnam, 74.1%. In contrast to this, other studies from developing countries recorded varying prevalences of 20% to 50% MRSA which are less than Papua New Guinea(Cosgrove et al., 2003; Mehta et al., 1998; Pai et al., 2010). European and American hospitals recorded prevalences ranging from 25% to 35% (Tiwari, Sapkota, & Sen, 2008). However, (Mejia et al.,

2010)reported greater than 50% MRSA prevalence in the United States. Those prevalences varied due to many factors. Overall, the literature indicates that prevalence of MRSA varies geographically and across different countries, whether developed or developing. Table 1 shows a summary of regional prevalence rates of MRSA. MRSA prevalence in this study setting is higher than the other regions. However, it should be noted that these various studies were done at different times using different methodologies.

In addition, some of the common factors causing the increase of HAIs caused by MRSA that were observed across hospitals worldwide included: overuse and misuse of antimicrobials; lack of surveillance and monitoring systems; low awareness; ineffective infection control measures; and weak health systems (Anupurba et al., 2003; Kumari, Mohapatra, & Singh, 2008; Mehta et al., 1998; Moet et al., 2007; Pai et al., 2010; Rajaduvaipandi et al., 2006). Furthermore, Haddadin et al. (2002) reported the risk factors for MRSA colonisation and infection, which are : advanced age; male gender; previous hospitalisation; length of hospitalisation; stay in an intensive care unit (ICU); chronic medical illness; presence and size of wound; exposure to colonised or infected patients; and presence of invasive catheter devices.

The factors causing the high prevalence of MRSA in this study maybe similar to the ones faced worldwide, mainly in developing countries. This current study reported increases in MRSA prevalence rates in pus swabs mainly from wounds (8.2%) and from catheter tips (1.3%) (see Table 3). The following factors could have been responsible for this high prevalence: the indiscriminate use of antibiotics; and lack of infection control (WHO,2017). As can be seen from the current study results, such a prevalence is alarmingly high compared to the other countries.

The five years (2012-2016) covered by the data examined this study saw variations in the prevalence of MRSA. An interesting finding was from the year 2013 to 2014 (see Figure 3). There was a significant increase of 9.8% compared to the previous year. The possible explanation for this increase would be ineffective infection control strategies in the hospital. There is an infection control unit in existence at the Port Moresby General Hospital; however, its efficiency is questionable. There are annual audits on

infection control; however, records are not found online, nevertheless, there are manual and electronic copies kept in the hospital. In addition, there was a study on the outbreak of nosocomial sepsis in the special care nursery in 2009that was caused by *Klebsiella pneumoniae*.The recommendation from that study was an urgent need for improved infection control strategies (Lithgow & Kilalang, 2009).After 2009, through the subsequent years up to 2016, there was no literature on studies regarding infection control at the Port Moresby General Hospital. Surveillance carried out by World Health Organization (2009b) has shown that a lack of or ineffective infection control measures in hospitals give rise to HAIs.

Another possible explanation for the increase observed in this study could have been a lack of aseptic techniques used in the laboratory. Since the microbiology laboratory uses a conventional method of culturing micro-organisms, almost 100% of the work is performed manually. Scientists may have cross-contaminated culture plates resulting in this increase. Furthermore, from 2013 to 2014, there was a shortage of staff at the microbiology laboratory. The researcher can personally confirm that there was a shortage of staff; however, an advertisement for positions in the microbiology laboratory to justify this claim in those years could not be retrieved. However, according to a United Nations International Children's Emergency Fund (UNICEF)annual report in 2014, there was shortage of staff in all health sectors across Papua New Guinea, including Port Moresby General Hospital (United Nation's Children's Emeregency Fund [UNICEF], 2014) . This shortage of staff led to overwork which may have caused scientists to ignore using aseptic techniques at times. For example, a scientist may not heat a wire loop thoroughly for culturing specimens onto an agar plate or for inoculation, thus causing cross-contamination of MRSA to another specimen. Further investigation could scrutinise whether a lack of aseptic techniques in the laboratory contributed to the increasing prevalence of MRSA. However, MRSA is known to be present in these environments, such as work benches in a laboratory (Stefani & Gogilo, 2010).Therefore, the possibility that the laboratory may have been responsible for the increase of MRSA cannot be ruled out. Further research may be able to verify this. Until then, the risk factors that have been discussed in comparison with the literature may have been the causes of the high prevalence of MRSA found in this study.

MRSA frequency differed across the months of the year (see Table 4).On average, the months of December to March saw increases in the prevalence of MRSA. The wet season falls around the months of December to March in Papua New Guinea. However, the prevalence varied in the five years between wet and dry seasons. No significant trend was recorded. Studies have reported seasonality variations in the prevalence of MRSA and *Staphylococcus aureus* infections (Leekha, Diekema, & Perencevich, 2012; Mermel, Machan, & Parenteau, 2011). In the wet or rainy season, there appears to be an increase in infections caused by MRSA as opposed to the dry season (Mermel, Machan & Parenteau,2011). The prevalence of MRSA infections or colonisation in different seasons may be attributed to the following factors: temperature, humidity and precipitation (Leekha et al., 2012).The current study did not report the prevalence of each infection by month to indicate a trend across the months of the year, as reported in most of the relevant literature; however, this study reported an overall prevalence of MRSA by month. Therefore, a trend for MRSA prevalence among different months was not observed to indicate the season in which MRSA was most prevalent.

The prevalence of MRSA isolates among the different genders varied in the findings of the current study (see Table 2). This study found a high prevalence of MRSA in the male gender (52.6%) compared to females (47.1%). This is consistent with a study by Austin et al. (2003) in a developing country which reported high( 60%) prevalence of MRSA in the male gender. Another study in a developing country reported a prevalence 65.8%in males and 34.2%in females which is higher than the findings of this study (Madani et al., 2001). Furthermore, two other studies that reported high frequency of MRSA among the male gender indicated the following risk factors for the finding: prolonged use of indwelling catherization; male patients above 50 years of age; and previous hospitalisation (Austin et al., 2003; Kupfer, Jatzwauk, Monecke, Mobius, & Wuesten, 2010). Even though Kupfer et al. (2010) reported a significant risk factor for MRSA prevalence as the male gender, they concluded that further research may help confirm the aetiology of this finding. Yet, another study found a higher frequency of MRSA in nasal swabs in males (Gorwitz et al., 2008), and this study attributed it to the different ethnicity of patients, which it was not possible to investigate in the current study setting. By contrast, Akpaka et al. (2006) identified

gender as a non-risk factor for MRSA prevalence and, as reported by Ghaznavi-Rad et al. (2010) , as cited in Kali et al. (2013, p. 1981), a few studies have shown no significant association between gender and MRSA. As discussed, few reasons were offered in the literature regarding prevalence of MRSA among the different gender. Therefore, in this present study it is not possible to hypothesize or make a confirmation as to the reason for this high prevalence in the male gender.

MRSA prevalence varies among different age groups in hospitals worldwide. In the current study findings, MRSA was high among the age groups 0-5 (39.9%) and 20-39 (28.8%) respectively (see Figure 4). Most literature, however, disagrees with these findings. Most reported high prevalence of MRSA in the older age groups (≥ 60 years) and those admitted in ICUs. The lowest prevalence of MRSA in this study was observed in patients ≥60 years (2.6%) and those in the ICU accounted for only 5.8%. This is also in agreement with studies in Nepal and Switzerland by Kumari et al. (2008) and Monnet et al. (2004). Klevens et al. (2006) in their survey, reported higher prevalence of MRSA in patients ≥ 65 years. However, this prevalence was acquired from ICUs only. ICUs are for patients who are critically ill, therefore the susceptibility to infections of persons in that age groups is high, and hence the higher prevalence. Furthermore, older patients and neonates have a weak immune system and when hospitalised, they are susceptible to HAIs caused by MRSA (World Health Organization, 2014b). As for this study the same could not be said, as patients of all age groups were considered. Even though persons greater than 60 years old are prone to acquiring infections, in this study, this was not so, most probably due to the low frequency of patients in that age group 60+ from the ICU (See Figure 4). Otherwise, this study would have given a different result consistent with the others in literature. This finding may indicate that infection control measures are effective in the ICUs and specialised wards including the special care nursery, TB clinic and labour wards at Port Moresby General Hospital.

This study reported a high prevalence of 73.4 % MRSA in swab specimens (see Table 3). The swab specimens were mainly from wound and skin infections. This finding is in accordance with other studies that found higher prevalence of MRSA in swab specimens (Gitau, Masika, Musyoki, Museve, & Mutwiri, 2018; Pai et al., 2010; Rajaduvaipandi et al., 2006; Tiwari et al., 2009). Rajaduvaipandi et al. (2006) reported a prevalence of 33.6% from pus swabs whilst Tiwari et al. (2009) recorded a total

prevalence of 71% from pus swabs and aspirates. (Kumari et al., 2008) reported a maximum isolation of 26.6% MRSA from pus and wound swabs; however, the total sample size was less than in the current study. Another recent study in Yemen also reported high MRSA prevalence in swab specimens (Alyahawi, Alkaf, & Alhomidi, 2018).*Staphylococcus aureus* is the major cause of wound infections (World Health Organization, 2014a). Swabs tend to have high isolation due to the normal flora of *Staphylococcus aureus* on the skin. When patients are hospitalised, their immune system becomes weakened, thus allowing for colonisation of MRSA, therefore leading to the observed increase of MRSA in swabs. All this increase is again attributed to lack of infection control and hygiene on the wards. Another important issue that has arisen from literature is whether all patients isolated with MRSA should be kept in isolation rooms. Surgical wards need effective post-operative hygiene policies or isolation protocols for patients isolated with MRSA. However, the finding of the present study concurs with most reported in literature, and therefore it can be concluded that our surgical wards will need effective infection control measures to reduce the burden of HAIs caused by MRSA.

Blood specimens had the second highest frequency of MRSA (see Table 3). The World Health Organization (2014c) concluded from their national surveys that it was common for patients with blood infections to have a high prevalence of MRSA in hospitals. Tiwari et al. (2008) reported a high prevalence of MRSA in pus specimens, with the next highest being blood specimens. Furthermore, a study conducted in India also reported the second highest prevalence of MRSA was in blood specimens(Joshi et al., 2013).The findings in this present study are on a par with other studies in developing countries (Pai et al., 2010; Rajaduvaipandi et al., 2006; Sadsad et al., 2013; Tiwari et al., 2009). The increase of MRSA in blood in this study would possibly be related to a lack of infection control measures at the site of collection and in the laboratory as well. Contaminants have been isolated from blood cultures many times, such contaminations occur due to lack of proper antiseptic techniques being used at the time of collection and a lack of infection control at the wards(Weinstein, 2003). Other times, contaminants are from the laboratory's end. Often, the growth on cultures at the laboratory do not correspond to the clinical diagnosis written on laboratory forms. That raises a concern about whether the MRSA is a true pathogen from a patient or a

contaminant from the laboratory. Failure to adhere to aseptic techniques in the laboratory gives rise to the growth of contaminants on culture plates.

However, in the years 2015 and 2016, there was a decrease in MRSA in blood specimens (see Table 6).This happened concurrently with the introduction of BACTEC (Bacton Dickinson automated blood culture system). The BACTEC machine was able to shorten turnaround times by indicating the growth of organisms faster, whether it be contaminants in the laboratory or true pathogens. However, it was not possible to clearly point out if this helped reduce MRSA. Nonetheless, it may be presumed that it helped indicate if aseptic techniques were not used at the collection point when there were growths of contaminants. The BACTEC has a 99% sensitivity and validity as opposed to the conventional method of culturing blood which has a 97% sensitivity and validity (Alizadeh, Movahed, & Mohammadnia, 2016; Weinston, 1996). Nevertheless, the conventional method has been the accepted method used worldwide.

The increase of bacteraemia in hospitals involves two major consequences, which are mortality and longer hospital stays. Firstly, proper effective control measures at a hospital help curb the increase of MRSA bacteraemia (Speller et al., 1997). Cosgrove et al. (2005) reported a high percentage of deaths due to MRSA caused by bacteraemia in a hospital in the US. This study did not capture the mortality rates of patients with bacteraemia caused by MRSA, however caution is required, nonetheless with respect to bacteraemia caused by MRSA. Secondly, longer hospital stays were reported by Cosgrove et al. (2005) for patients with MRSA bacteraemia. It cost the hospital between$US5000 and$US20,000 for patients with MRSA bacteraemia. Bacteraemia caused by MRSA puts a financial strain on a hospital when patients stay longer. If many patients were to stay longer in the hospital, it will have an immense effect and financially drain the hospital. The cost would be unbearable. Unfortunately, this study did not gather data on the number of days of admission, which would be needed to be able to make a definite statement on the costs involved. Nevertheless, more surveillance is needed on rates of infections caused by MRSA.

In the United Kingdom, surveillance programmes were created to capture and monitor data on bacteraemia caused by MRSA (Johnson et al., 2005).This surveillance included

the number of days patients spent in the hospitals. This enabled them to confirm factors causing an increase in MRSA bacteraemia and put effective measures in place to reduce the prevalence of MRSA bacteraemia. This study reported second highest prevalence of MRSA in blood which is consistent with a number of other studies (Dibah, Arzanlou, Jannati, & Shapouri, 2014; Johnson et al., 2005; Speller et al., 1997).Therefore, all the measures discussed in the preceding paragraphs which were; monitoring of infections caused by MRSA and effective infection control measures have to be considered and implemented to reduce bacteraemia caused by MRSA.

The specimen type with the lowest frequency of MRSA reported in this study was CSF. This finding corroborates a study in eastern Nepal by Kumari et al. (2008).However, the cause of low MRSA rates in CSF is not clearly stated in literature. The possible explanations for the low prevalence in this study were: treating patients prior to doing a lumbar puncture (the invasive procedure used for collecting CSF) and having no growths on CSF cultures. Also, MRSA in the CSF is a serious infection that is less likely to occur than one through a skin cut. CSF is a sterile specimen, and thus, most times, yields no growths. Furthermore, most CSF specimen came from paediatric patients, and(World Health Organization, 2014a) statistics found that MRSA meningitis was only rarely known to occur in children as compared to other organisms such as *Haemophilus influenzae* and *Streptococcus pneumoniae*.

This study reported a maximum isolation of 26.7% MRSA from the surgical wards (see Figure 5).The surgical wards had most post-operative wound infections, hence the high prevalence. This is consistent with a study in India that isolated the highest rate of MRSA from pus samples from the surgical wards (Tyagi, Kapil, &Singh, 2008). Another study by Hussain et al. (2005) reported 39% of MRSA from the surgical wards which was somewhat higher than this current study finding. Furthermore, in a collective surveillance study by (World Health Organization, 2014c), it was found that surgical wards are known to have high prevalence of MRSA. In contrast, however, others found a higher prevalence of MRSA in ICUs (Haddadin et al., 2002; Klavs et al., 2003).

The possible reasons for the high prevalence of MRSA on the surgical wards in this study were: lack of infection control and lack of patient isolation which causes cross-infection and overcrowding. These factors, lack of infection control and overcrowding,

are consistent with studies conducted in India (Anupurba et al., 2003; Pai et al., 2010; Rajaduvaipandi et al., 2006). However, there is yet another factor believed to cause MRSA infections in surgical wards, which is a patient's previous history of hospitalization. It was not possible to ascertain whether patients had previous hospitalisation in this present study. As Samad, Banerjee, Carbarns, and Ghosh (2001) reported, most patients do not remember dates of previous admissions, thus, to confirm whether MRSA was hospital-acquired or community-acquired was difficult. Effective infection control measures may be the main strategy to reduce MRSA in surgical wards (Samad et al., 2001).

The locations with the lowest frequency of MRSA reported in the present study were the TB Clinic (0.1 %) and the labour wards (0.1 %). The possible reason for low frequency in the TB clinic is that it is an isolated clinic for TB patients only, therefore it is always kept clean and has effective infection control measures. Furthermore, there are other medications and practices in place in a TB ward, thus the low frequency of MRSA in the TB wards. There is emphasis on infection control in order to avoid patients getting opportunistic infections which may impose additional financial constraints on the hospital and could be fatal. Thus, the same emphasis on infection control is practised in the labour ward; it is a sterile ward for delivery as babies are prone to infections.

MRSA was favourable to skin infections, recording a prevalence of 45.6 % (see Table 5).This result reflects those across Asia and India that reported high prevalence of hospital-acquired MRSA in skin infections and soft tissue (Alrabiah et al., 2016; Bell & Turnidge, 2002; Chen & Huang, 2014; Molton et al., 2013). *Staphylococcus aureus* is a normal skin flora therefore it is not surprising to have a high prevalence in skin infections. In contrast, Fluit, Wielders, Verhoef, and Scmitz (2001) reported a low prevalence of MRSA in skin and soft tissue infections. This low frequency of MRSA in skin and soft tissue infections in that study were attributed to prolonged antibiotic treatment of severely ill patients. What is unclear is whether this high prevalence is entirely hospital acquired. In the United States, community-acquired MRSA(CA-MRSA)is now a common cause of skin infections (Langi et al., 2009).A note of caution is due here since our study did not specify whether patients were admitted for 48hours or more, as this is defined by CDC as the threshold for infections to be identified as

HAIs. However,in the literature, HA-MRSA did have a much higher prevalence in many hospitals compared to CA-MRSA.

This study reported 74.1% of MRSA isolates were obtained from in-patients whilst for out-patients the figure was 24.3%. Joshi et al. (2013) reported similar findings to this current study. They found 85% MRSA from in-patients and 28% from out-patients in 2008, and 96% MRSA from in-patients and 27% from out-patients in 2009. In another study in Saudi Arabia,Baddour, Abuelkheir, and Fatani (2006) reported similar findings, with 77.5% of MRSA obtained from in-patients and 22.5% from out-patients. In contrast to this, in the United States, a higher prevalence of MRSA was reported in out-patients than in-patients (Styers, Sheehan, Hogan, & Sahm, 2006). A possible explanation for the findings in this study would be that the number of in-patients was higher than out-patients (see Table 7), thus there was a greater chance of isolating MRSA from in-patients. Another possible reason would be the length of hospitalisation in wards, rendering patients susceptible to catching HAIs.

### 5.2.2 Sensitivity patterns of MRSA

With respect to the second research question, MRSA sensitivity patterns recorded in this study are consistent with findings from other studies (Joshi et al., 2013; Pai et al., 2010; Rajaduvaipandi et al., 2006; Tiwari et al., 2008). All confirmed *Staphylococcus aureus* tested were methicillin resistant. Confirmation of MRSA was made using cefoxitin (30µg) and oxacillin (1µg) discs (see Table 13). Both cefoxitin and oxacillin are recommended by CLSI (2013) and EUCAST (2013) for confirmation of MRSA. Oxacillin had been used for decades before the introduction of cefoxitin.However, some find cefoxitin to be a more reliable choice than oxacillin. CDC (2013) recommends cefoxitin to be a better choice than oxacillin, as cefoxitin gives more accurate and reproducible results. More recently, Velasco et al. (2005) have proven cefoxitin to be a reliable diagnostic disc for the confirmation of MRSA. They used PCR which was the gold standard test. The validity was 100% compared to oxacillin which was 98%. In addition, others have found that the oxacillin disk diffusion method is the least reliable method for detection of methicillin resistance (Chambers, 1997; York, Gibbs, Chehab, & Brooks, 1996). Oxacillin has been found to have a low sensitivity and validity for confirming MRSA (Chambers, 1997; Velasco et al., 2005). Even though it was recommended in the past, organisms have developed certain resistant strains, therefore continuous

evaluation must be carried out to find the most suitable diagnostic disc for MRSA confirmation. In the current study findings, oxacillin was used whenever the cefoxitin disc was unavailable. This approach to testing may be open to scrutiny; however, for now, it can be stated that both diagnostic discs in the data collected for this study confirmed MRSA. Nonetheless, in future the confirmation discs used need to be on par with what is recommended and used around the world. Further research using PCR maybe be required to confirm the best diagnostic disc for confirmation of MRSA in Port Moresby General Hospital.

MRSA was highly sensitive to vancomycin (95.5%) and tetracycline (92.7%) in this study. The findings of this study are consistent with similar studies in India (Anupurba et al., 2003; Joshi et al., 2013; Rajaduvaipandi et al., 2006; Tiwari et al., 2009; Tiwari et al., 2008). In addition, Akpaka et al. (2006) found 100% sensitivity to vancomycin in Trinidad and Tobago. Vancomycin belongs to the glycopeptide class of antibiotics which makes it a higher antibiotic; therefore, most organisms including MRSA tend to be sensitive towards vancomycin. However, Chen and Huang (2014) reported higher resistance to vancomycin in South-east Asia. Vancomycin-resistant *Staphylococcus aureus* (VRSA) was problematic in that region. Furthermore,Assadullah, Kakru, Bhat, Hussain, and Shah (2003) found that, though sensitivity to vancomycin was high, caution should be observed in treating patients colonised with MRSA with vancomycin, as it is a glycopeptide. Being a glycopeptide, vancomycin has adverse effects such as nephrotoxicity,oxotoxicity and thrombophlebitis (Yoshida,Matzno,Namba,Nishikata & Matsuyama,2006).Therefore, instead, increased doses of beta-lactams should be considered as another possibility to decrease chances of resistance developing due to the overuse of vancomycin. Based on this advice, caution should be observed in the use of vancomycin in our hospital, in order to avoid resistance to vancomycin developing. This is further justified by studies from India that saw emergence of vancomycin-resistant MRSA (Assadullah et al., 2003; Tiwari & Sen, 2006). Then again, vancomycin is the drug of choice used widely to treat MRSA infections. Low vancomycin resistance has been reported recently, therefore caution must be observed in its use (Centres for Disease Control and Prevention [CDC], 2014; Kaleem, Usman, Hassan, Omair, & Uddin, 2010; Kali et al., 2013). All in all, finding the best

treatment option is not the only strategy; however continuous surveillance of both pathogenic organisms and antibiotic use should be adhered to.

Tetracycline is another higher antibiotic classified under the broad-spectrum antibiotics thus, high prevalence (80%) was observed as well. The finding of this current study is in agreement with others (Joshi et al., 2013; Pai et al., 2010; Rajaduvaipandi et al., 2006; Tiwari et al., 2009). Even though these studies were not necessarily the same as this current study in terms of methodology and statistical techniques used, the high percentage of tetracycline observed was necessary for comparison. In contrast, Anupurba et al. (2003) and Kaleem et al. (2010) reported higher resistance of MRSA to tetracycline. However others reported that more use of broad spectrum antibiotics may cause MRSA to become resistant (Summaiya, Manish, Latika, & Geeta, 2007).Furthermore tetracyclines are bacteriostatic and should not be used for treatment of endocarditis, intravascular diseases or CNS infections(Long, Pickering, & Prober, 2012).

MRSA showed higher resistance to erythromycin with 27.1% and chloramphenicol with 20.6% (see Table 5) in this current study. This is quite different to a study in India by Anupurba et al. (2003) which reported a resistance to erythromycin of greater than 80%. Tiwari et al. (2008)also reported a high resistance to erythromycin in their study in Northern India. Pai et al. (2010) reported a high resistance of 40-50% to erythromycin. In addition, increasing resistance to erythromycin was reported in South-east Iran (Sadeghi & Mansouri, 2013), to the extent that it was no longer prescribed by clinicians. One further study in India reported a resistance to erythromycin of 54.3% (Sharma, Garg, Baliga, & Bhat, 2013),which is only a moderate resistance when compared to similar studies that reported higher frequencies of resistance.

Skin infections were predominant with MRSA, hence the high resistance to erythromycin in this study. Erythromycin is mainly prescribed for skin infections; thus, overuse may cause MRSA strains to develop resistance (CDC,2013;WHO,2014a) Another possible explanation for the high resistance to erythromycin would have been over-prescribing. Because erythromycin is used to treat different skin infections, a culture may not have been requested prior to treating with erythromycin.

This current study found a highly significant (*p=0.019*) association between the antibacterial chloramphenicol (30µg) and gender (see Table 14). The rate of chloramphenicol sensitive MRSA was higher in males and in females also. This significance among the different genders and chloramphenicol could be related to three factors which Meibohm, Beierle, and Derendorf (2002) stated as drug absorption, distribution and metabolism. There is scant literature with which to make comparisons; however, when considering all antibiotics, a knowledge of the pharmacology and pharmacokinetics is vital to shed light on the significant finding reported here. This significance is possibly related to the body mass of the different genders. Males generally have a larger body mass thus metabolism of chloramphenicol would be slower, which is confirmed in our findings with males having high resistance to chloramphenicol. Again, an understanding of the pharmacokinetics and pharmacodynamics of antibiotics is crucial for clinicians in the treatment of MRSA, or any other infection for that matter. In addition, Meibohm et al. (2002) further reiterated that "gender-related differences are an important determinant of the clinical effectiveness of drug therapy" (p. 32).

In the current study's findings, females showed higher sensitivity (82.5%) to chloramphenicol than males (76%). The World Health Organization (2011)found, in its national surveys, that the metabolism of chloramphenicol varies with age, gender and clinical conditions .Generally, females have a smaller body mass compared to males, thus metabolism of chloramphenicol is faster, thereby causing the high sensitivity. In addition, chloramphenicol is well absorbed by neonates and infants (World Health Organization, 2014c),thus explaining the significance of the finding as most MRSA isolates were from the paediatric population.

Patients presenting with different clinical conditions respond differently to antibiotics. In this study, highly significant associations were observed between all clinical infections and the antibacterial erythromycin with a significance of *p=0.006* and septrin with p*=0.001* (see Table 15 and Table 16). In a study in the United States, the significant association for erythromycin was attributed to the different clinical strains present (Klevens et al., 2006). In the finding in the present study, this maybe a possibility; however, the determination of the different strains of MRSA is not possible in the laboratory. It may mean that different clinical conditions respond differently to

erythromycin. One clinical condition that was prevalent in this study was skin infections and, as noted earlier, erythromycin is the choice of drug for skin infections. Skin infections were predominant in this study therefore the significance is relevant. WHO(2011) reported different clinical conditions having different sensitivities to certain antibacterials.

Septrin is also widely used as a first-line antibiotic to treat most clinical infections. Septrin has different sensitivities across hospitals worldwide(F. Gould et al., 2009). Septrin showed moderate sensitivity and a low resistance rate (see Table 16) in the current study's findings. Though most literature reported the use of septrin as a first-line antibiotic, the sensitivity has not been clearly stated. In contrast to the current study finding, one study reported high resistance to septrin (I. M. Gould et al., 2012). Septrin is recommended for treating MRSA infections in many hospital settings World Health Organization (2014c).Almost all infections showed sensitivity to septrin. There was a significant association (*p=0.001*) between clinical infections and septrin (see Table 16). This significant association indicated that septrin is used as a first-line antibiotic in the Port Moresby General Hospital. An interesting finding from a previous study reported the use of septrin as a more cost-effective antimicrobial than vancomycin (Bishara et al., 2003).

There was a significant association between different clinical specimens and the antibiotics chloramphenicol (*p=0.001*) and septrin (*p=0.001*) (see Table 17 and Table 18) in this study. This is a highly significant result. This result does not correlate with any findings in the literature; however, could be an important finding to report, as different specimen types may respond differently to chloramphenicol and septrin. The only significant association that was explained was the association between different clinical infections and the antibacterial, not so much the different specimens.

## 5.3 Conclusion

There seem to have been a progressive increase in the prevalence of MRSA at the Port Moresby general hospital in Papua New Guinea for the five years from 2012 to 2016.It is quite high as compared to other developing countries. There is a need for surveillance of the prevalence and antimicrobial profile of MRSA. Many factors were

responsible for this high prevalence of MRSA which, as discussed, included lack of infection control and lack of effective prevention strategies.

The surgical wards reported a high frequency of MRSA. This indicated the lack of infection control measures on the surgical wards. Effective infection control measures must be formulated mainly for the isolation of infected persons and post-operative wound infections.

The clinical infections with highest frequency were the skin infections followed by blood infections. All these findings were all attributed to the above-mentioned factors.

The age groups with the high frequency of MRSA were those between 0-5 years old. This is alarmingly and needs urgent attention particularly the infection control strategies in the paediatric wards and monitoring of antibiotics prescribed to patients in the above mentioned age groups.

In terms of the sensitivity patterns, the findings reported here were consistent with studies around world. MRSA has becoming increasingly resistant to erythromycin and septrin, whilst still highly sensitive to vancomycin and tetracycline. Although vancomycin is the drug of choice for MRSA infections, a study of VRSA should be conducted in the future. The most commonly used antibiotics were septrin and erythromycin, hence the resistance to them. However, continued indiscriminate use of antibiotics and non-surveillance of antibiotic use will spiral into a different sensitivity pattern in the next 10 years or so.

The factors commonly reported in the literature for the high prevalence of MRSA and varied antimicrobial sensitive patterns include non-surveillance of antibiotics, over-prescribing and lack of effective prevention and control strategies.

## 5.4 Strengths of the study

This study was able to document the prevalence of MRSA in Papua New Guinea in a referral hospital, which has never been done before. This study may be used as a reference for future studies. The status of MRSA prevalence compared with the prevalence worldwide has been documented. The susceptibility pattern of MRSA has been described as well. This study indicated the need for effective infection control policies and monitoring of antimicrobial use.

## 5.5 Limitations of the study

All retrospective studies have some form of bias and limitations. The major limitations encountered in this study were: missing records from log books and missing anti-staphylococcal agents. However, these issues did not significantly affect the results. Another limitation was the non-availability of full panel of antibiotics. The data on antimicrobial susceptibility patterns were not uniform with most reported in literature. Furthermore, missing data which was needed for a good comparison of the antimicrobial susceptibility was encountered. Time was also a limitation in obtaining antimicrobial susceptibility patterns of MSSA in order to be able to make a comparison. The time frame given to collect data was only three months. Again, this did not affect the outcome very much. Another possible area for further research is whether CA-MRSA was prevalent as well. However, this study did partially substantiate the fact that out-patients may have brought MRSA from the community. Another limitation observed was the lack of previous literature on MRSA prevalence in the Pacific region and Papua New Guinea. A prospective study would have given a different perspective on MRSA prevalence and sensitivity patterns.

## 5.6 Recommendations

The findings of this thesis have led to the following recommendations:

- Port Moresby General Hospital should come up with effective hand-hygiene measures. As discussed, skin infections were predominant compared to other infections .Therefore, a policy on hand hygiene, if already in place, should be reviewed, evaluated and monitored to assess its effectiveness.

- There should be continuous and effective surveillance of the usage of correct antibiotics for MRSA or any other MDROs. Again, the trend of susceptibility patterns should be observed and reviewed regularly to monitor changes and point out likely causes of variations. An antimicrobial stewardship programme should be created at the PMGH. The departments and groups that should be involved include:
  - the pharmacy department, which should monitor drugs prescribed for MRSA infections from different wards and the clinical conditions associated with MRSA;

  - clinicians on the wards, who should follow a treatment guideline book for the correct antibiotics for MRSA alone; and
  - the laboratory, which should continuously monitor MRSA isolates and have a protocol in place for alerting clinicians.

  A cost-effective empirical therapy policy should be formulated in the form of a standard treatment guideline.

- Universal MRSA screening for both patients and staff may also help reduce HA-MRSA in the hospital. The hospital should make separate budget for MRSA screening for both patients and staff.

- All clinical infections should be monitored at the laboratory end and causative organisms like MRSA should be monitored and reported monthly if this is not already being done. Quarterly reports should be given to responsible authorities in the hospital for action to reduce MRSA.

- A review of the antimicrobial testing for MRSA should be conducted and only one standard antimicrobial susceptibility testing guideline should be used, one that is commonly used at the present time, either CLSI or EUCAST.

- Healthcare workers should be screened regularly for MRSA. The hospital prevalence of MRSA includes both patients and healthcare providers.

- The findings have provoked thoughts about future research. One future investigation that would be vital is to determine the exact phenotype of MRSA present in the Port Moresby General Hospital, Papua New Guinea. Secondly, several study sites in Papua New Guinea should be employed to give a correct representation of the antimicrobial susceptibility patterns of MRSA in Papua New Guinea. Future research should concentrate on the prospective or molecular studies of MRSA strains and their epidemiology. A database should be created in conjunction with the WHO and the CDC in Papua New Guinea to monitor antimicrobial susceptibility patterns of MRSA.

## 5.7 Concluding statement

MRSA is dangerous and a global public health problem and needs to be monitored carefully and reduced in any hospital. MRSA cannot be completely eradicated but may be reduced. Port Moresby General Hospital could greatly reduce MRSA within five years if all the recommendations presented here are implemented, monitored, and accomplished.

# References

Aglua, I., Nombri, J., Drekore, J., Poka, H., & Michael, A. (2018). Methicillin-resistant *Staphylococcus aureus* in Melanesian children with hematogenous osteomyelitis from the central highlands of Papua New Guinea. *International journal of paediatrics, 6*(10), 8361-8370. https://doi.org/10.22038/ijp.2018.31279.2763

Aia.P, Lavu, E., John, L. N., Johnson, K., Coulter, C., Ershova, J., . . . Islam, T. (2016). The burden of drug-resistant Tuberculosis in Papua New Guinea:Results of a large Population-Based Survey. *PLOS ONE*. https://doi.org/https://doi.org/10.1371/journal.pne.0149806

Akpaka, P. E., et al. (2006). Prevalence and antimicrobial susceptibility pattern of methicillin-resistant *Staphylococcus aureus* isolates from Trinidad and Tobago. *Annals of Clinical Microbiology and Antimicrobials***5**(16): 1-6.

Alekshun, M. N., & Levy, S. B. (2007). Molecular mechanisms of antibacterial multi-drug resistance. *Cell, 6*(23), 1037-1050. https://doi.org/https://doi.org/10.1016/j.cell.2007.03.004

Alizadeh, A. M., Movahed, R. K., & Mohammadnia, M. (2016). Comparative evaluation of conventional and BACTEC methods for detection of bacterial infection. *Tanaffos, 15*(2), 112-116.

Allegranzi, B., & Pittet, D. (2009). Role of hand-hygiene in health-care associated infection prevention. *journal of hospital infection, 73*(4), 305-315. https://doi.org/https://doi.org/10.1016/j.jhin.2009.04.019

Alrabiah, K., Alola, S. A., Banyan, E. A., Al Shaalan, M., & Al Johani, S. (2016). Characteristics and risk factors of hospital acquired-Methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infection of pediatric patients in a tertiary care hospital in Riyadh,Saudi Arabia. *International journal of pediatrics and adolescent medicine, 3*(2), 71-77. https://doi.org/https://doi.org/10.1016/j.ijpam.2016.03.006

Alyahawi, A., Alkaf, A., & Alhomidi, A. M. (2018). Prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) and antimicrobial susceptibility patterns at a private hospital in Sana'a Yemen. *Universal journal of pharmaceutical research, 3*(3), 4-9. https://doi.org/https://doi.org/10.22270/ujpr.v313.159

Anupurba, S., Sen, M. R., Nath, G., Sharma, B. M., Gulati, A. K., & Mohapatra, T. M. (2003). Prevalence of methicillin resistant staphylococcus aureus in a tertiary referral hospital in eastern Uttar Pradesh. *Journal of medical microbiology, 21*(1), 49-51.

Appelbaum, P. C. (2006). MRSA-the tip of the iceberg. *Clinical microbiology and infection, 12*(S2), 3-10. https://doi.org/https://doi.org/10.1111/j.1469-0691.2006.01402.x

Appelbaum, P. C. (2007). Microbiology of antibiotic resistance in *Staphylococcus aureus*. *Clinical infectious diseases, 45*(S3), S165-S170. https://doi.org/https://doi.org/10.1086/519474

Archer, G. L. (1998). *Staphylococcus aureus*:A well-armed pathogen. *Clinical infectious diseases, 26*, 1179-1181. https://doi.org/https://doi.org/1086/520289

Asa, H., Laman.M, & Greenhill, A. R. (2012). Bloodstream infections caused by resistant bacteria in surgical patients admitted to Modilon Hospital,Madang. *Papua New guinea medical journal*(1-4), 5-11.

Assadullah, S., Kakru, D. K., Bhat, F. A., Hussain, N., & Shah, A. (2003). Emergence of low level vancomycin resistance in MRSA. *Indian journal of medical microbiology, 21*(3), 196-198.

Atilano, M. A. G., Pena, A. C., Chua, J. A., & Coronel, R. F. (2001). Prevalence of Methicillin-resistant *Staphylococcus aureus* and Methicillin-resistant coagulase negative *Staphylococcus aureus* in a tertiary hospital. *Philladelphia journal of microbiology and infectious diseases, 30*(4), 126-132.

Austin, T. W., Austin, M. A., Mclear, D. E., Coleman, B. T., Osoba, A. O., Thaqafi, A. O., & Lamfon, M. A. (2003). MRSA prevalence in a teaching hospital in Western Saudi Arabia. *Saudi medical journal, 24*(12), 1313-1316. https://doi.org/https://www.researchgate.net/publication/8930567

Baird, D. (Ed.). (1996). *Cluster forming gram positive cocci: Mackie and McCartney Practical medical microbiology* (4th ed.). New York: Churchill living stone.

Barnes, T., & Jinks, A. (2008). Methicillin-resistant *Staphylococcus aureus*:the modern day challenge. *British journal of nursing, 17*(16), 1012-1018.

Aia, P., Lavu, E., John, L. N., Johnson, K., Coulter, C., Ershova, J., . . . Islam, T. (2016). The burden of drug-resistant Tuberculosis in Papua New Guinea:Results of a large Population-Based Survey. *PloS One*. https://doi.org/https://doi.org/10.1371/journal.pne.0149806

Akpaka, P. E., Kissoon, S., Swanston, W. H., & Monteil, M. (2006). Prevalence and antimicrobial susceptibility pattern of methicillin-resistant *Staphylococcus aureus* isolates from Trinidad and Tobago. *Annals of Clinical Microbiology and Antimicrobials, 5*(16), 1-6. https://doi.org/https://doi.org/10.1186/1476-0711-5-16

Alekshun, M. N., & Levy, S. B. (2007). Molecular mechanisms of antibacterial multi-drug resistance. *Cell, 6*(23), 1037-1050. https://doi.org/https://doi.org/10.1016/j.cell.2007.03.004

Alizadeh, A. M., Movahed, R. K., & Mohammadnia, M. (2016). Comparative evaluation of conventional and BACTEC methods for detection of bacterial infection. *Tanaffos, 15*(2), 112-116.

Allegranzi, B., & Pittet, D. (2009). Role of hand-hygiene in health-care associated infection prevention. *Journal of Hospital Infection, 73*(4), 305-315. https://doi.org/https://doi.org/10.1016/j.jhin.2009.04.019

Alrabiah, K., Alola, S. A., Banyan, E. A., Al Shaalan, M., & Al Johani, S. (2016). Characteristics and risk factors of hospital acquired-Methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infection of pediatric patients in a tertiary care hospital in Riyadh,Saudi Arabia. *International Journal of Pediatrics and Adolescent Medicine, 3*(2), 71-77. https://doi.org/https://doi.org/10.1016/j.ijpam.2016.03.006

Alyahawi, A., Alkaf, A., & Alhomidi, A. M. (2018). Prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) and antimicrobial susceptibility patterns at a private hospital in Sana'a Yemen. *Universal journal of pharmaceutical research, 3*(3), 4-9. https://doi.org/https://doi.org/10.22270/ujpr.v313.159

Ansari, F., Erntell, M., Goossens, H., & Davey, P. (2009). The European surveillance of antimicrobial consumption (ESAC) point -prevalence survey of antibacterial use in 20 European hospitals in 2006. *Clinical Infectious Diseases, 49*(10), 1496-1504. https://doi.org/https://10.1086/644617

Anupurba, S., Sen, M. R., Nath, G., Sharma, B. M., Gulati, A. K., & Mohapatra, T. M. (2003). Prevalence of methicillin resistant staphylococcus aureus in a tertiary referral hospital in eastern Uttar Pradesh. *Journal of Medical Microbiology, 21*(1), 49-51.

Appelbaum, P. C. (2006). MRSA-the tip of the iceberg. *Clinical Microbiology and Infection, 12*(S2), 3-10. https://doi.org/https://doi.org/10.1111/j.1469-0691.2006.01402.x

Appelbaum, P. C. (2007). Microbiology of antibiotic resistance in *Staphylococcus aureus*. *Clinical Infectious Diseases, 45*(S3), S165-S170. https://doi.org/https://doi.org/10.1086/519474

Archer, G. L. (1998). *Staphylococcus aureus*:A well-armed pathogen. *Clinical Infectious Diseases, 26*, 1179-1181. https://doi.org/https://doi.org/1086/520289

Assadullah, S., Kakru, D. K., Bhat, F. A., Hussain, N., & Shah, A. (2003). Emergence of low level vancomycin resistance in MRSA. *Indian Journal of Medical Microbiology, 21*(3), 196-198.

Atilano, M. A. G., Pena, A. C., Chua, J. A., & Coronel, R. F. (2001). Prevalence of Methicillin-resistant *Staphylococcus aureus* and Methicillin-resistant coagulase negative *Staphylococcus aureus* in a tertiary hospital. *Philladelphia journal of microbiology and infectious diseases, 30*(4), 126-132.

Austin, T. W., Austin, M. A., Mclear, D. E., Coleman, B. T., Osoba, A. O., Thaqafi, A. O., & Lamfon, M. A. (2003). MRSA prevalence in a teaching hospital in Western Saudi Arabia. *Saudi Medical Journal, 24*(12), 1313-1316. https://doi.org/https://www.researchgate.net/publication/8930567

Baddour, M. M., Abuelkheir, M. M., & Fatani, A. J. (2006). Trends in antibiotic susceptibility patterns and epidemiology of MRSA isolates from several hospitals in Riyadh,Saudi Arabia. *Annals of Clinical Microbiology and Antimicrobials, 5*(30), 1-11. https://doi.org/10.1186/1476-0711-5

Baird, D. (Ed.). (1996). *Cluster forming gram positive cocci: Mackie and McCartney Practical medical microbiology* (4th ed.). New York: Churchill living stone.

Barnes, T., & Jinks, A. (2008). Methicillin-resistant *Staphylococcus aureus*:the modern day challenge. *British Journal of Nursing, 17*(16), 1012-1018.

Bauer, K. A., West, J. E., Balada-Llasat, J., Pancholi, P., Stevenson, K. B., & Goff, D. A. (2010). An antimicrobial stewardship program's impact. *Clinical Infectious Diseases, 51*(9), 1074-1080. https://doi.org/https://doi.org/10.1086/656623

Beam, J. W., & Buckley, B. (2006). Community-acquired Methicillin resistant Staphylococcus aureus: Prevalence and risk factors. *Journal of athletic training,, 41*(3), 337-340.

Bell, J. M., & Turnidge, J. D. (2002). High prevalence of oxacillin-resistant *Staphylococcus aureus isolates* from hospitalized patients in Asia-Pacific and South-Africa:Results from Sentry Antimicrobial surveillance program 1998-1999. *Antimicrobial Agents and Chemotherapy, 62*(7), 880-882. https://doi.org/10.1128/AAC.46.3.880-882

Bishara, J., Pitlik, S., Samra, Z., Levy, I., Paul, M., & Leibovici. (2003). Co-trimoxazole-sensitive,Methicillin-resistant *Staphyloccus aureus*,Israel,1988-1997. *Emerging Infectious Diseases, 9*(9), 1168-1169. https://doi.org/10.3201/eid0909.020666

Boucher, H. W., & Corey, G. R. (2008). Epidemiology of Methicillin-resistant *Staphylococcus aureus*. *Clinical Infectious Diseases, 5*, 344-349. https://doi.org/https://doi.org/10.1086/533590

Bouchiat, C., El-Zeenni, N., Chakrakodi, B., Nagaraj.S., Arakere, G., & Etienne, J. (2015). Epidemiology of Staphylococcus aureus in Bangalore, India: emergence of the ST217 clone and high rate of resistance to erythromycin and ciprofloxacin in the community. *New microbes and new infections 7*, 15-20. https://doi.org/doi:10.1016/j.nmni.2015.05.003

Boyce, J. M., Cookson, B., Chriatiansen, K., Hori, S., Vuopio-Varkila, J., Kocagoz, S., . . . Pittet, D. (2005). Methicillin-resistant *Staph.aureus*. *The lancet infectious disease, 5*(10), 653-663. https://doi.org/https://doi.org/10.1016/S1473-3099(05)70243-7

Centres for Disease Control [CDC]. (2017). *CDC MRSA*. Retrieved from https://www.cdc.gov/mrsa/tracking/index.html

Centres for Disease Control and Prevention. (2010). *MRSA infections.* Retrieved from www.cdc.gov/mrsa

Centres for Disease Control and Prevention [CDC]. (2013a). *CDC in Papua New Guinea*. Retrieved 02.10, 2018, from

https://www.cdc.gov/globalhealth/countries/papua-new-guinea/pdf/papua-new-guinea.pdf

Centres for Disease Control and Prevention [CDC]. (2013b). *MRSA infections*. Retrieved April 4, 2018, from www.cdc.gov/mrsa

Centres for Disease Control and Prevention [CDC]. (2014). *Active bactetrial core surveillance report,emreging infections program network,Methicillin-resistant Staphylococcus aureus ,2014*. Retrieved November 6, 2018, from http://www.cdc.gov/abcs/reports-findings/surveyreports/mrsa.14.html

Centres for Disease Control and Prevention [CDC]. (2018). *Health -care associated infections (HAI)*. Retrieved November 23, 2018, from https://www.cdc.gov/hai/data/index.html

Chambers, H. F. (1997). Methicillin-resistant in *Staphylococci*:Molecular and biochemical basis and clinical implications. *Clinical Microbiology Reviews, 10*(4), 781-792. https://doi.org/10.1128/CMR.10.4.781

Chambers, H. F. (2001). The changing epidemiology of *Staphylococcus aureus?Emerging Infectious Diseases, 7*(2), 178-182.

Chen, C. J., & Huang, Y. C. (2014). New epidemiology of Staphylococcus aureus in Asia. *Clinical Microbiology and Infection, 20*(7), 605-623. https://doi.org/https://doi.org/10.1111/1469.0691.12705

Clinical and Laboratory Standards Institute [CLSI]. (2013). *CLSI guidelines.* Retrieved from https://clsi.org

Clinical Laboratory Standards Institute [CLSI]. (2013). *Performance standards for antimicrobial susceptibility testing.CLSI approved standard M100-S23.Clinical and Laboratory standards*. PA: Wayne.

Coello, R., Glynn, J. R., Gaspar, C., Picazo, J. J., & Fereres, J. (1997). Risk factors for developing clinical infection with methicillin-resistant *Staphylococcus aureus* (MRSA) amongst hospital patients initially colonized with MRSA. *The journal of hospital infection, 37*(1), 39-46. https://doi.org/https://doi.org/10/SO195-670(97)90071-2

Coia, J., Duckworth, G., & Edwards, D. (2006). Guidelines for the control and prevention of MRSA in healthcare facilities. *Journal of hospital infections, 63*(1), 1-44.

Coombs, G. W., Nimmo, G. R., Pearson, J. C., Christiansen, K. J., Bell, J. M., Collignon, P. J., & McLaws, M. (2009). Prevalence of MRSA strains among *Staphylococcus aureus* isolated from outpatients,2006. *Communicable Diseases Intelligence Quarterly Report, 33*(1), 10-20.

Cosgrove, S. E., Qi, Y., Kaye, K. S., Harbarth, S., Karchmer, A. W., & Carmeli, Y. (2005). The impact of methicillin resistance in Staphylococcus aureus bacteraemia on patient outcomes: Mortality, length of stay, and hospital charges. *Infect Control Hospital Epidemiology 26*, 166-174.

Cosgrove, S. E., Sakoulas, G., Perencevich, E. N., Schwaber, M. J., Karchmer, A. W., & Carmeli, Y. (2003). Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteraemia:a meta-analysis. *Clinical Infectious Diseases, 36*(1), 53-59. https://doi.org/https://doi.org/10.1086/345476

Couto, I., Melocristino, J., Fernandes, T., Garcia, N., Serrano, M. J., Salgado, A., . . . deLencastre, H. (1995). Unusually large number of methicillin resistant Staphylococcus aureus clones in Portuguese hospital. . *Journal of Clinical Microbiology, 33*, 2032-2035.

Cox, R. A., Conquest, C., Mallaghan, C., & Marples, R. R. (1995). A major outbreak of methicillin resistant Staphylococcus aureus caused by a new phage type (EMRSA-16). *Journal of Hospital*

*Infection, 29*(22), 87–106.

Cresswell, J. W. (2014). *Research design:Qualitative,quantitative and mixed approach* (5th eds ed.). Washington,DC: Sage.

Crossley, K. B., & Arthur, G. L. (1997). The Staphylococci in human disease. *Public Health, 111*(6), 435-435. https://doi.org/https://doi.org/10.1038/sj.ph.1900409

Daniel, W. W. (1999). *Biostatistics: A Foundation for Analysis in the Health Sciences.* Denver,USA: John Wiley & Sons.

Dibah, S., Arzanlou, M., Jannati, E., & Shapouri, R. (2014). Prevalence and antimicrobial resistance pattern of methicilllin resistant *Staphylococcus aureus* (MRSA) strains isolated from clinical specimens in Ardabil,Iran. *Iranian journal of microbiology, 6*(3), 163-168.

Diekema, D. J., Bootsmiller, B. J., Vaughn, T. E., Woolson, R. F., Yankey, J. W., Ernst, E. J., . . . Doebbeling, B. N. (2004). Antimicrobial resistance trends and outbreak

frequency in United States hospitals. *Clinical Infectious Diseases, 38*(1), 78-85. https://doi.org/https://doi.org/10.1086/380457

Dilnessa, T., & Bitew, A. (2016). Prevalence and antimicrobial susceptibility pattern of methicillin resistance Staphylococcus aureus isolated from Yekatit 12 Hospital Medical College,Addis

Ababa,Ethiopia. *Infectious Diseases, 16*. https://doi.org/10.11/s12879-016-1742-5

Engemann, J. J., Carmeli, Y., Cosgrove, S. E., Fowler, V. G., Bronstein, M. Z., Trivette, S. L., . . . Kaye, K. S. (2003). Adverse clinical and economic outcomes attributable to methichillin-resistant among patients with *Staphylococcus aureus* surgical site infection. *Clinical Infectious Diseases, 36*(5), 592-598. https://doi.org/https://doi.org/10.1086/367653

Enright, C., Robinson, D. A., Randle, G., Feil, E. J., Grundmann, H., & Spratt, B. G. (2002). The evolutionary history of methicicllin-resistant *Staphylococcus aureus* (MRSA). *Proceedings of the National Academy of Sciences of the United States of America, 99*(11), 7687-7692. https://doi.org/https://doi.org/10.1073/pnas.122108599

Enright, M. C. (2003). The evolution of a resistant pathogen-the case of MRSA. *Current Opinion in Pharmacology, 3*, 474-479. https://doi.org/10.1016/1471-4892(003)00109-7

European Centre for Disease Prevention and Control [ECDCP]. (2018). *Surveillance and disease data*. Retrieved 29th July,2018, from https://ecdc.europa.eu

European Centre for Disease Prevention and Control [ECDPC]. (2013). *Annual epidemiological report,2011*. Retrieved from https://ecdc.europa.eu

European Committee on Antimicrobial Susceptibility Testing [EUCAST]. (2013). *Antimicrobial susceptibility testing*. Retrieved December 20, 2018, from www.eucast.org/ast_of_bacteria/

Euser, A. M., Zoccali, C., Jager, K. J., & Dekker, F. W. (2009). Cohort studies:Prospective versus retrospective. *Nephron clinical practice, 113*, 214-217. https://doi.org/10.1159/000235241

Falagas, M. E., Karageorgopoulos, D. E., Leptidis, J., & Korbila, I. P. (2013). MRSA in Africa:Filling the global map of antimicrobial resistance. *PloS One, 8*(7), 1-12. https://doi.org/https://doi.org/10.1371/journal.pone.0068024

Ferguson, J. (2015). *Antimicrobial resistance and Papua New Guinea*. Retrieved from https://pdfs.semanticsscholar.org/.../00e70b554631f9e920a9b8e8ffba36195bf5.pdf

Fluit, A. C., Wielders, C. L. C., Verhoef, J., & Scmitz, F. J. (2001). Epidemiology and susceptibility of 3,051 *Staphylococcus aureus* isolates from 25 University hospitals participating in the European SENTRY study. *Journal of Clinical Microbiology, 39*(10), 3727-3732. https://doi.org/10.1128/JCM.39.10.3727-3732.2001

Gad, G. F. M., El-Gafaar, A., El-Domany, R. A. A., & Hashem, Z. S. (2010). Epidemiology and antimicrobial resistance of staphylococci isolated from different infectious diseases. *Brazillian journal of microbiology, 41*(2), 333-334. https://doi.org/10.1590/S1517-838220100002000012

Ghaznavi-Rad, E., Shamsudin, M. N., Sekawi, Z., Khoon, L. Y., Aziz, M. N., Hamat, R. A., . . . Neela, V. (2010). Predominance and emergence of Clones of Hospital-Acquired Methicillin-resistant *Staphylococcus aureus* in Malaysia. *Journal of Clinical Microbiology, 48*, 867-872. https://doi.org/10.7860/JCDR/2013/6142.3377

Gitau, W., Masika, M., Musyoki, M., Museve, B., & Mutwiri, T. (2018). Antimicrobial susceptibility pattern of *Staphylococcus aureus* isolates from clinical specimens at Kenyatta National Hospital. *BMC Research Notes, 11*, 226. https://doi.org/10.1186/s13104-018-3337-2

Goethebeur, M., Landry, D., Han, D., & Vicente, C. (2006). Methicillin-reistant *Staphylococcus aureus*:A public health issue with economic consequences. *Canadian journal of infectious diseases and medical microbiology, 18*(1), 27-34. https://doi.org/https://dx.doi.org/10.1155/2007/253947

Gordon, R. J., & Lowly, F. D. (2008). Pathogenesis of Methicillin-resistant *Staphylococcus aureus* infection. *Clinical Infectious Diseases, 46*(5), 350-359. https://doi.org/https://doi.org/10.1086/533591

Gorwitz, R. J., Kruszon-Morgan, D., McAllister, S. K., McQuillan, G., McDougal, L. K., Fosheim, G. E., . . . Kuehnert, M. J. (2008). Changes in the nasal colonization with *Staphylococcus aureus* in the United States,2001-2004. *Thejournal of infectious disease, 197*(9), 1226-1234. https://doi.org/https://doi.org/10.1086/533494

Gould, F., Brindle, R., Chadwick, P. R., Fraise, A. P., Hill, S., Nathwani, D., . . . Spry, M. J. (2009). Guidelines for the pophylaxis and treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the United Kingdom. *Journal of Antimicrobial Chemotherapy, 63*(5), 849-861. https://doi.org/https://doi.org/10.1093/jac/dkp065

Gould, I. M. (2008). The epidemiology of antibiotic resistance. *International Journal of Antimicrobial Agents, 32*(1), 2-9. https://doi.org/https://doi.org/10.1016/j.ijantimicag.2008.06.016

Gould, I. M., David, M. Z., Esposito, S., Garau, J., Lina, G., Mazzei, T., & Peters, G. (2012). New insights into methicillin-resistant *Staphylococcus aureus*(MRSA) pathogenesis,treatment and resistance. *Journal of Antimicrobial Agents, 39*(2), 96-104.

Grundmann, H., Aanensen, D. M., Wijngaard, C. C., Spratt, B. G., Harmsen, & Friedrich, A. W. (2010). Geographical distribution of *Staphylococcus aureus* causing Invasive infections in Europe:A molecular-epidemiological analysis. *PLoS Biology, 7*(1), 1-15.

Haddadin, A. S., Fappiano, S. A., & Lipsett, P. A. (2002). Methicillin-resistant *Staphylococcus aureus* in the intensive care unit. *Postgraduate Medical Journal, 78*, 385-392. https://doi.org/https://dx.doi.org/10.1136/pmj.78.921.385

Harbarth, S., Fankhauser, C., & Schrenzel, J. (2008). Universal screening for Methicillin-resistant *Staphylococcus aureus* at hospital admission and nosocomial infection in surgical patients. *JAMA, 299*(10), 1149-1157. https://doi.org/10.1001/jama.299.10.1149

Hardy, K. J., Oppenheim, B. A., Gossain, S., Gao, F., & Hawkey, P. M. (2006). A study of the relationship between environmental contamination with Methicillin-resistant *Staphylococcus aureus* (MRSA) and patients's acquisition of MRSA. *Infection Control and Hospital Epidemiology, 27*(2), 127-132. https://doi.org/https://doi.org/10.1086/500622

Hassoun, A., Linden, P. K., & Friedman, B. (2016). Incidence, prevalence and management of MRSA bacteraemia across patient population- a review of recent developments in MRSA management and treatment. *Critical care, 21*(11). https://doi.org/https://doi.org/10.1186/S13054-017-1801-3

Health Protection Agency [HPA]. (2010). *MRSA information for patients*. Retrieved from https://www.gov.uk

Health Protection Agency [HPA]. (2013). MRSA information for patients.

Heffernan, H., & Bakker, S. (2016). Annual survey of Methicillin-resistant Staphylococcus aureus (MRSA), 2015. Nosocomial Infections, Institute of Environmental Science and Research Limited.

Hiramatsu, K., Katayam, Y., Yuzawa, H., & Ito, T. (2002). Molecular genetics of methicillin-resistant *Staphylococcus aureus International Journal of Medical Microbiology, 292*, 67-74.

Hryniewicz, W. (1999). Epidemiology of MRSA. *Infection, 27*(13), 14-16.

Hussain, S., Shams, R., Ahmad, K., Perveen, R., & Riaz, B. (2005). Prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) in surgical site infections in a tertiary care hospital. *International journal of pathology, 3*(2), 81-85.

Inhorn, M. C. (1995). Medical anthropology and epidemiology:Divergences or convergences? *Medical anthropology and epidemiology, 40*(3), 285-290.

Institute of Environmental Science and Research [IESR]. (2012). *Antimicrobial data from hospital and community laboratories*. Retrieved 25.01., 2019, from https://surv.esr.cri.nz/antimicrobial/general_antimicrobial_susceptibility

Institute of Environmental Science and Research limited [IESR]. (2008). *Antimicrobial resistance data from hospital and community laboratories*. Retrieved from www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/AR/National_AR_2008.pdf

Jarvis, W. R., Jarvis, A. A., & Chinn, R. Y. (2012). National prevalence of methicillin-resistant Staphylococcus aureus in inpatients in United states healthcare facilities,2010. . *American Journal of Infection Control, 40*(3), 194-200. https://doi.org/doi:10.1016/j.ajc.2012.02.001

John, R., Naraqi, S., & McDonnel, G. (1990). The clinical spectrum of staphylococcal bacteraemia:a review of 101 Melanesian patients from Papua New Guinea. *Papua New Guinea Medical Journal, 33*(3), 229-233.

Johnson, A. P., Pearson, A., & Duckworth, G. (2005). Surveillance and epidemiology of MRSA bacteraemia in the UK. *Journal of Antimicrobial Chemotherapy, 56*(3), 455-462. https://doi.org/https://doi.org/10.1093/jac/dki266

Jones, M. E., Mayfield, D. C., Thornsberry, C., Karlowsky, J. A., Sahm, D. F., & Peterson, D. (2002). Prevalence of oxacillin resistance in *Staphylococcus aureus* among

inpatients in the United States during 2000. *Antimicrobial agents and chemmotherapy, 46*(9), 3104-3105. https://doi.org/10.1128/AAC.46.9.3104-3105.2002

Joshi, S., Ray, P., Manchanda, V., Bajaj, J., Chitnis, D. S., Gautam, V., . . . Balaji, V. (2013). Methicillin-resistant Staphylococcus aureus (MRSA) in India: Prevalence and susceptibility pattern. *Indian Journal of Medical Research, 137*(2), 363-369.

Kaleem, F., Usman, J., Hassan, A., Omair, M., & Uddin, R. (2010). Sensitiviy pattern of methicillin-resistant *Staphylococcus aureus* isolated from patients admitted in a tertiary care hospital of Pakistan. *Iranian journal of microbiology, 2*(3), 141-143.

Kali, A., Stephen, S., Umadevi, S., Kumar, S., Joseph, N. M., & Srirangaraj, S. (2013). Changing trends in resistance pattern of Methicillin-resistant *Staphylococcus aureus*. *Journal of clinical and diagnostic research, 7*(9), 1979-1982. https://doi.org/10.7860/JCDR/2013/6142.3377

Kaya, Y. (2013). Comparison of quantitative and qualitative research traditions:epistemological,theoretical and methodological differences. *European journal of education, 48*(2), 311-324. https://doi.org/https://doi.org/10.1111/ejed.12014

Kejela, T., & Bacha, K. (2013). Prevalence and antibiotic susceptibility pattern of methicillin-resistant

Staphylococcus aureus among primary school children and prisoners in Jima Towu Southwest

Ethiopia. *Annals of Clinical Microbiology and Antimicrobials, 12*(11). https://doi.org/doi:10.1186/1476-0711-12-11

Kesah, C., Redjeb, S. B., Odugbemi, T. O., Boye, C. S. B., Dosso, M., Achola.J.O, . . . Borg, M. (2003). Prevalence of methicillin-resistant Staphylococcus aureus in eight African hospitals and Malta. *Clinical Microbiology and Infection, 9*(2), 153-156. https://doi.org/10.1046/j.1469-0691.2003.00531.x

Klavs, I., Luznik, B., Skerl, M., Grgic-Vitek, M., Zupanc, L., Dolinsek, M., . . . Arnez, Z. (2003). Prevalence and risk factors for hospital-acquired infections in SLovenia-results of the first national survey,2001. *Journal of Hospital Infection, 54*, 149-157. https://doi.org/https://doi.org/10.1016/S0195-6701(03)00112-9

Klevens, R. M., Edwards, J. R., Tenover, F. C., McDonald, L. C., Horan, T., & Gaynes, R. (2006). Changes in the epidemiology of Methicillin-Resistant *Staphylococcus aureus* in Intensive Care Units in US Hospitals,1992-2003. *Clinical Infectious Diseases, 42*(3), 389-391. https://doi.org/https://doi.org/1086/499267

Klevens, R. M., Morrison, M. A., Nadle, J., Petit, S., Gershman, K., Ray, S., . . . Fridkin, S. K. (2007). Active Bacterial Core surveillance (ABCs) MRSA Investigators: Invasive methicillin resistant *Staphylococcus aureus* infections in the United States. *JAMA, 298*, 1763–1771

Knight, G. M., Budd, E. L., Whitney, L., Thornley, A., Al-Ghusein, H., Planche, T., & Lindsay, J. A. (2012). Shift in dominant-hospital associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) clones over time. *Journal of Antimicrobial Chemotherapy, 67*(10), 2514-2522. https://doi.org/https://doi.org/10.1093/jac/dks245

Kumari, N., Mohapatra, T. M., & Singh, Y. I. (2008). Prevalence of methicillin-resistant Staphylococcus aureus (MRSA) in a tertiary care hospital in Eastern Nepal. *Journal of Nepal medical association, 47*(170), 53-63.

Kupfer, M., Jatzwauk, L., Monecke, S., Mobius, J., & Wuesten, A. (2010). MRSA in a large German University Hospital:Male gender is a significant risk factor for acquisition. *GMS Krankenhaushygiene interdisziplinar, 5*(2), 1-8. https://doi.org/doi:10.3205/dgkh000154

Langi, S. A. P., Robinson, J. O., Pearson, J. C., Christiansen, K. J., Coombs, G. W., & Murray, R. J. (2009). Intrafamilial Transmission of Methicillin-Resistant *Staphylococcus aureus Emerging Infectious Diseases, 15*(10), 1687-1689. https://doi.org/10.3201/eid1510.081532

Leekha, S., Diekema, D. J., & Perencevich, E. N. (2012). Seasonality of staphylococcal infections. *Clinical Microbiology and Infection, 18*(10), 927-933. https://doi.org/https://doi.org/10.1111/j.1469-0691.2012.03955.x

Ley, S. D., Riley, I., & Beck, H.-P. (2014). Tuberculosis in Papua New Guinea:from yesterday until today. *Microbes and infection, 16*, 607-614. https://doi.org/https://doi.org/10.1016/j.micinf.2014.06.012

Lithgow, A. E., & Kilalang, C. (2009). Outbreak of nosocomial sepsis in the Special Care nursery at Port Moresby general hospital due to multiresistant *Klebsiella pneumoniae*: high impact on mortality. *PNG medical journal, 52*(1-2), 28-34.

Long, S. S., Pickering, L. K., & Prober, C. G. (2012). *Pediatric infectious diseases* (4th ed.). Philadelphia,USA: Elsevier.

Lowly, F. D. (1998). *Staphylococcus aureus* infections. *The new England journal of medicine, 339*, 520-532. https://doi.org/10.1056/NEJM199808203390806

Madani, T. A., Al-Abdullah, N. A., Al-Sanousi, A. A., TGhabrah, T. M., Afandi, S. Z., & Bajunid, H. A. (2001). Methicillin-resistant *Staphylococcus aureus* in two tertiary care centres in Jeddah,Sauda Arabia. *Infection Control and Hospital Epidemiology, 22*(4), 211-216. https://doi.org/https://doi.org/10.1086/501891

Mann, C. J. (2003). Observational research methods.Research design:cohort,cross sectional and case-control studies. *Emergency Medicine Journal, 20*(1), 54-60. https://doi.org/http://dx.doi.org.exproxy.aut/ac.nz/10.1136/emj.20.1.54

Maragakis, L. L., Perencevich, E. N., & Cosgrove, S. E. (2014). Clinical and economic burden of antimiccrobial resistance. *Expert Review of Anti-Infective Therapy, 6*(5), 751-763. https://doi.org/https://doi.org/10.1586/14787210.6.5.751

Marimuthu, K., Pittet, D., & Harbarth, S. (2014). The effect of improved hand hygiene on nosocomial MRSA control. *Antimicrobial resistance and infection control, 3*(34). https://doi.org/doi:10.1186/2047-2994-3-34

Mcbryde, E. S., Bradley, L. C., Whitby, M., & McElwain, D. L. (2004). An investigation of contact transmission of methicillin-resistnat *Staphylococcus aureus*. *Journal of hospital infections, 58*(2), 104-108. https://doi.org/10.1016/j.jhin.2004.06.010

McDonald, M. (1997). The epidemiology of Methicillin-resistant *Staphylococcus aureus*:Surgical surveillance 20 years on. *Australia and New Zealand journal of surgery banner, 67*(10), 682-685. https://doi.org/https://doi.org/10.1111/j.1445-2197.1997.tb07108.x

Mehta, A. P., Rodrigue, C., Sheth, K., Jani, S., Hakimiyan, A., & Fazalbhoy, N. (1998). Control of methicillin-resistant *Staphylococcus aureus* in a tertiary care center. *Journal of Medical Microbiology, 16*(1), 31-34.

Meibohm, B., Beierle, I., & Derendorf, H. (2002). How important are gender differences in phamacokinetics. *Clinical Pharmacokinetics, 41*(5), 329-342.

Mejia, C., Zurita, J., & Guzman-Blanco, M. (2010). Epidemiology and surveillance of methicillin-resistnat *Staphylococcus aureus* in Latin America. *Brazillian journal of infectious diseases, 14*(2), 79-86. https://doi.org/10.1016/j.ijantimicag.2009.06.005

Mermel, L. A., Machan, J. T., & Parenteau, S. (2011). Seasonality of MRSA infections. *PloS One, 6*(3), 1-5. https://doi.org/https://doi.org/10.1371/journal.pone.0017925

Ministry of health. (2016). *Public health surveillance.Information for New Zealand Public Helath Action*. Retrieved 25.01., 2019, from https://www.surv.esr.cri.nz/antimicrobial/mrsa_annual.php

Moellering, R. C. (2012). MRSA:the first century. *Journal of Antimicrobial Chemotherapy, 67*, 4-11. https://doi.org/doi:10.1093/jac/dkr437

Moet, G. J., Jones, R. N., Biedenbach, D. J., Stilwell, M. G., & Fritsche, T. R. (2007). Contemporary causes of skin and soift tissue infections in North America,Latin America and Europe:Report from the SENTRY antimicrobial surveillance program (1998-2004). *Diagnostic Microbiology and Infectious Disease, 57*(1), 7-13. https://doi.org/https://doi.org/10.1016/j.diagmicrobio.2006.05.009

Molton, J. S., Tambayah, P. A., Ang, B., Ling, M. l., & Fisher, D. A. (2013). The global spread of Health-Care Associated - Multidrug resistant bacteria: A perspective from Asia. *Clinical infectious diseases, 56*(9), 1310-1318.

Monnet, D. L., MacKenzie, F. M., Lopez-Lozano, J., Bayaert, A., Camacho, M., Wilson, R., . . . Gould, I. M. (2004). Antimicrobial drug use and methicillin-resistant *Staphylococcus aureus*,Aberdeen,1996-2000. *Emerging Infectious Diseases, 10*(8), 1432-1441. https://doi.org/doi.10.3201/eid1008.020694

Mouton, J. W., Brown, D. F. J., Apfalter, P., Canton, R., Giske, C. G., Ivanova, M., . . . Kahlmeter, G. (2011). The role of pharmacokinetics/pharmacodynamics in setting clinical MIC breakpoints: the EUCAST approach. *Clinical microbiology infection 18*, 37-45. https://doi.org/10.11114/j.1469-0691.2011.03752.x

Mulligan, M. E., Murray-Leisure, K. A., Ribner, B. S., Standiford, H. C., John, J. F., Korvick, J. A., . . . Yu, V. L. (1993). Methicillin-resistant *Staphylococcus aureus*:A consensus review of the microbiology,pathogenesis and epidemiology with implications for prevention and management. *The American journal of medicine, 94*(3), 313-328. https://doi.org/https://doi.org/10.1016//0002-9343(93)-U

National Department of Health [NDOH]. (2010). *National health plan 2011-2020:Policies and strategies*. Retrieved August 4, 2018, from www.wpro.who.int

National Nosocomial Infections Surveillance [NNIS]. (2004). NNIS system report, data summary from January 1992 through June 2004. *American Journal of Infection Control, 32*(8), 470-485. https://doi.org/doi:10/1016/50196655304005425

National Statistical Office [NSO]. (2011). *Final figures 2011 census*. Retrieved 20.06.2018, from https://www.nso.gov.pg

Nickerson, E. K., West, T. E., Day, N. P., & Peacock, S. J. (2009). Staphylococcus aureus and drug resistance in resource limited countries in south and east Asia. *Lancet Infectious Diseases, 9*, 131-135.

Nimmo, G. R., Pearson, J. C., Collignon, P. J., Christiansen, K. J., Coombs, G. W., Bell, J. M., & McLaws, M. (2007). Prevalence of MRSA among *Staphylococcus aureus* isolated from hospitlal inpatients,2005: Report from the Australian gropup for antimicrobial resistance *Communicable Diseases Intelligence Quarterly Report, 31*(3), 288-296.

Office for National Statistics (ONS). (2017). *Trends in MRSA in England and Wales*. Retrieved from https://www.ons.gov.uk

Organisation for Economic Co-operation and Development [OECD]. (2016). *Antimicrobial resistance is a growing health and economic threat requiring a multipronged response*. Retrieved 20.09.2018, from www.oecd.org/els/health-systems/antimicrobial-resistance.htm

Ortwine, J. K., & Bhavan, K. (2018). Morbidity,mortality and management of methicillin-resistant *S.aureus* in the USA:update on antibacterial choices and understanding. *Journal of hospital practice, 46*(2), 64-72. https://doi.org/https://doi.org/10.1080/21548331.2018.1435128

Pai, V., Rao, V., & Rao, S. (2010). Prevalence and antimicrobial susceptibility pattern of methicillin-resistant Staphylococcus aureus (MRSA) isolate at a tertiary care hospital in Mangalore, South India. *Journal of laboratory physicians 2*(2). https://doi.org/doi:10.4103/0974-2727-72155

Pallant, J. (2010). *SPSS survival manual: A step by step guide to data analysis using IBM SPSS* (5th ed.). New York: McGraw Hill.

Papua New Guinea's information. (n.d.). Retrieved 21st July, 2018, from https://worldatlas.com/webimage/countrys/oceania/papuanewguinea/pgland.htm

Pearce, N. (2012). Classification of epidemiological study designs. *International Journal of Epidemiology, 41*(2), 393-397. https://doi.org/https://doi.org/10.1093/ije/dys049

Perry, J. D., Davies, A., Butterworth, A., Hopley, A. L. J., Nicholson, A., & Gould, K. F. (2004). Development and evaluation of chromogenic agar medium for methicillin resistant Staphylococcus aureus. *Journal of Clinical Microbiology, 42*(10), 4519-4523. https://doi.org/10.1128/JCM.42.10

Pittet, D. (2001). Improving adherence to hand hygiene practice: Multidisciplinary Approach. *Emerging Infectious Diseases, 7*(2), 234-240.

Pourhoseingholi, M. A., Valedi, M., & Rahimzadeh, M. (2013). Sample size calculation in medical statistics. *Journal of gastroenterology and hepatology from bed to bench, 6*(1), 14-17.

Rajaduvaipandi, K., Mani, K. R., Paneerselvam, K., Mani, M., Bhaskar, M., & Manikandan, P. (2006). Prevalence and antimicrobial susceptibility pattern of methicillin resistant Staphylococcus aureus: A multicentre study. *Indian Journal of Medical Microbiology, 24*(1), 34-38. https://doi.org/10.4103/0255-0857.19892

Roghmann, M., Siddiqui, A., Plaisance, K., & Standiford, H. (2001). MRSA colonization and the risk of MRSA bacteraemia in hospitalized patients with chronic ulcers. *Journal of Hospital Infection, 47*(2), 98-103. https://doi.org/doi:10.1053/jhin.2000.0903

Ronald, J. N. (1967). Resistance patterns among nosocomial pathogens:Trends over the past few years. *Hospital-acquired infections:Realities of risks and resistance, 119*(2), 397-404. https://doi.org/https://doi.org/10.1378/chest_suppl.397S

Ronald, J. N. (2001). Resistance patterns among nosocomial pathogens:trends over the past few years. *Chest, 119*(S2), 397S-404S.

Sadeghi, J., & Mansouri, S. (2013). Molecular characterization and antibiotic resistance of clinical isolates of methicillin-resistant *Staphylococcus aureus* obtained from South-east of Iran (Kerman). *Journal of microbiology and immunology, 122*, 405-411. https://doi.org/https://doi.org.10.1111/apm.12158

Sadsad, R., Sintchenko, V., Mcdonnel, G. D., & Gilbert, G. L. (2013). Effectiveness of Hospital-wide Methicillin-resistant *Staphylococcus aureus* (MRSA) infection

control policies differs by ward specilaity. *PloS One, 8*(12), 1-8. https://doi.org/10.1371/journal.pone.0083099

Saikia, L., Nath, R., Choudhury, B., & Sakar, M. (2009). Prevalence and antimicrobial susceptibility pattern of methicillin-resistant Staphylococcus aureus in Assam. *Indian journal of critical care medicine, 13*(3), 156-158. https://doi.org/10.4103/0972-5229.58542

Samad, A., Banerjee, D., Carbarns, N., & Ghosh, S. (2001). Prevalence of methicillin-resistant *Staphylococcus aureus* colonization in surgical patients,on admission to a Welsh hospital. *Journal of Hospital Infection, 51*, 43-46. https://doi.org/doi:10.1053/jhin.2002.1182

Shariq, A., Tanvir, S. B., Zaman, A., Khan, S., Anis, A., Khan, M. A., & Ahmed, S. (2017). Susceptibility profile of methicillin-resistant *Staphylococcus aureus* to linezolid in clinical isolates. *International Journal of Health Sciences, 11*(1), 1-4.

Sharma, N. K., Garg, S., Baliga, S., & Bhat, K. G. (2013). Nosocomial infections and drug susceptibility patterns in methicillin sensitive and methicillin resistant *Staphylococcus aureus*. *Journal of clinical & diagnostic research, 7*(10), 2178-2180. https://doi.org/10.7860/JCDR/2013/6750.3463

Shorr, A. F. (2007). Epidemiology and economic impact of methicillin-resistant *Staphylococcus aureus*:review and analysis of the literature. *Pharmcoeconomics, 25*(9).

Shurland, S., Zhan, M., Bradham, D. D., & Roghmann, M. (2015). Comparison of mortality risk associated bacteremia due to Methicillin-resistant and Methicillin-Susceptible Staphylococcus aureus. *Infection Control and Hospital Epidemiology, 28*(3), 273-279. https://doi.org/https://doi.org/10.1086/512627

Sit, P., Ju-Teh, C. S., Idvis, N., Sam, I., Omar, S. F., Sulaiman, H., . . . Ponnampalavanar, S. (2017). Prevalence of methicillin-resistant Staphylococcus aureus (MRSA) infection and the molecular characteristics over a 2 years period in a tertiary teaching hospital in Malaysia. *BMC infectoius diseases, 17*, 274-278. https://doi.org/10.1186/s12879-017-2384-y

Skov, R., Larsen, A., Kearns, A., Holmes, M., Teale, C., Edwards, G., & Hill, R. (2014). Phenotypic detection of mecC-MRSA:cefoxitin is more reliable tha n oxacillin. *Journal of Antimicrobial Chemotherapy, 69*(1), 133-135. https://doi.org/https://doi.org/10.1093/jac/dkt341

Song, J. H., Hsueh, P. R., Chung, D. R., Ko, K. S., Kang, C. I., Peck, K. R., . . . Hung, V. P. (2011). Spread of methicillin-resistant *Staphy*lococcus aureus between the community and the hospitals in Asian countries:An ANSORP study. *Journal of Antimicrobial Chemotherapy, 66*(5), 1061-1069.

Song, J. W., & Chung, K. C. (2011). Observational studies:Cohort and case control studies. *Plastic reconstruction surgery, 126*(6), 2234-2242. https://doi.org/doi:10.1097/PRS.Ob013e3181f44abc

Speller, D. C. E., Johnson, A. P., James, D., Marples, R. R., Charlett, A., & George, R. C. (1997). Resistance to methicillin and other antibiotics in isolates of *Staphylococcus aureus* from blood and cerebospinal fluid,England and Wales,1989-95. *The lancet, 350*(9074), 323-325. https://doi.org/https://doi.org/10/S0140-6736(97)12148-1

Stefani, S., Chung, D. R., Lindsay, J. A., Friedrich, A. W., Kearns, A. M., Westh, H., & Mackenzie, F. M. (2012). Methicillin-resistant *Staphylococcus aureus* (MRSA):global epidemiology and harmonisation of typing methods. *International Journal of Antimicrobial Agents, 39*(4), 273-282. https://doi.org/https://doi.org/10.1016/j.ijantimicag.2011.09.030

Stefani, S., & Gogilo, A. (2010). Methicillin-resistant *Staphylococcus aureus*: related infcetions and antibiotic resistance. *International Journal of Infectious Diseases, 14*(S4), S19-S22. https://doi.org/https://doi.org/10.1016.j.ijid.2010.05.009

Stone, P. W. (2009). Economic-burden of Healthcare-Associated infection: An American Perspective. *American Journal of Infection Control, 32*(8), 470-485.

Styers, D., Sheehan, D. J., Hogan, P., & Sahm, D. F. (2006). Laboratory-based surveillance of current antimicrobial resistance patterns and trends among *Staphylococcus aureus*:2005 status in the United States. *Annals of Clinical Microbiology and Antimicrobials, 5*(2), 1-9. https://doi.org/10.1186/1476-0711-5-2

Summaiya, M., Manish, P., Latika, S., & Geeta, V. (2007). Study of antibiotic sensitivity pattern of methicillin-resistant *Staphylococcus aureus*. *Indian Journal of Critical Care Medicine, 11*(2), 99-101.

Tenover, F. C. (2006). Mechanisms of antimicrobial resistance in bacteria. *American Journal of Infection Control, 34*(5), S3-S10. https://doi.org/https://doi.org/10.1016/j.ajic.2006.05.219

The Independent State of Papua New Guinea. (2011). *Papua New Guinea vision 2050*. Retrieved from www.treasury.gov.pg

The Independent State of Papua New Guinea. (2012). *Papua New Guinea Vision 2050*. Retrieved from www.treasury.gov.pg

The Statistical Portal. (n.d.). *Urbanization in Papua New Guinea*. Retrieved August 8, 2018, from https://www.statista.com/statistics/731765/urbanization-in-papua-new-guinea/

The World Health Report. (2000). *Improving performance*. Retrieved July,30, 2018, from https://www.wpro.who.int/chip/chip04/definitions.htm

Tiwari, H. K., Das, A. K., Sapkota, D., Sivarajan, K., & Pahwa, V. K. (2009). Methicillin-resistant *Staphylococcus aureus*: prevalence and antibiogram in a tertiary care hospital in western Nepal. *The journal of infection in developing countries, 3*(9), 681-684. https://doi.org/https://doi.org/10.3855/jidc.86

Tiwari, H. K., Sapkota, D., & Sen, M. R. (2008). High prevalence of multi-drug resistant MRSA in a tertiary care hospital of northern India. *Infection and drug resistance 1*, 57-61.

Tiwari, H. K., & Sen, M. R. (2006). Emergence of resistant *Staphylococcus aureus* (VRSA) from a tertiary care hospital from northern part of India. *BMC Infectious Diseases, 6*(156), 1-6. https://doi.org/doi:10.1186/1471-2334-6-156

Turnidge, J., & Paterson, D. L. (2007). Setting and revising antibacterial susceptibility breakpoints. *Clinical Microbiology Reviews, 20*(3), 391-408. https://doi.org/10.1128/CMR.00047-06

Tyagi, A., Kapil, A., &Singh, R. (2008). Incidence of methicillin resistant Staphylococccus aureus (MRSA) in pus samples at a tertiary care hospital,AIIMS,New Delhi. *Indian academy of clinical medicine, 9*(1), 33-35.

United Nation's Children's Emeregency Fund [UNICEF]. (2014). *UNICEF annual report 2014*. Retrieved 12.02.2019, from https://www.unicef.org/..../annualreport/.../Papua_New_Guinea_Report_2014....

Velasco, D., Tomas, M., Cartelle, M., Beceiro, A., Perez, A., Molina, F., . . . Bou, G. (2005). Evaluation of different methods for detecting methicillin-resistant (oxacillin) resistance in *Staphylococcus aureus*. *Journal of Antimicrobial*

*Chemotherapy, 55*(3), 379-382. https://doi.org/https://doi.org/10.1093/jac/dki017

Wareng, S. E., Foster, H. A., & Daw, M. A. (2014). Antimicrobial susceptibility patterns of methicillin-resistant Staphylococcus aureus isolates collected from healthcare and community facilities in Libya show a high level of resistance to fusidic acid. *Journal of infectious disease and therapy, 2*(189). https://doi.org/10.4172/2332-0877.100089

Weber, D. J., Raasch, R., & Rutala, W. A. (1999). Nosocomial infections in the ICU:The growing importance of antibiotic-resistant pathogens. *Nosocomial infections in the ICU, 115*(3), 34S -41S. https://doi.org/https://doi.org/10.1378/chest.115_1.34S

Weinstein, M. P. (2003). Blood culture contamination:persisting problems and partial progress. *Journal of Clinical Microbiology, 41*(6), 2275-2278. https://doi.org/10.1128/JCM.41.6.2275-2278.2003

Weinston, M. P. (1996). Current blood culture methods and systems:Clinical concepts,Technology, adn interpretation of results. *Clinical Infectious Diseases, 23*(1), 40-46. https://doi.org/https://doi.org/10.1093/clinids/23.1.40

Wernitz, M. H., Swidsinski, S., Weist, K., Sohr, D., Witte, W., Frank, K.-P., . . . Veit, S. K. (2005). Effectiveness of a hospital wide-selective screening programme for methicillin-resistant *Staphylococcus aureus* (MRSA) carriers at hospital admission to prevent hospital-acquired MRSA infections. *Clinical Microbiology and Infection, 11*(6), 457-465. https://doi.org/https://doi.org/10.1111/j.1469-0691.2005.01152.x

WHO Western Pacific Region. (2018). *Health information,evidence and research*. Retrieved August 4, 2018, from www.wpro.who.int

Wikipedia. (n.d.-a). *Papua New Guinea*. Retrieved 04.08.2018, from https://en.wikipedia.org

Wikipedia. (n.d.-b). *Port Moresby General Hospital*. Retrieved from https://en.wikipedia.org/wiki/Port_Moresby_General_Hospital

Williamson , D., Zhang, J., Ritchie, S. R. R., S.A, Fraser, J. D., & Baker, M. G. (2014). Staphylococcus aureus infections in New Zealand,2000-2011. *Emerging Infectious Diseases, 20*(7), 1156-1161. https://doi.org/10.3201/eid2007.1319234

World Health Organization. (2002). *Prevention of hospital acquired infections:a practical guide*. Retrieved from www.who.int

World Health Organization. (2006). *Epidemic and pandemic alert and response*. Retrieved from www.who.int

World Health Organization. (2009a). WHO guidelines on hand hygiene in health care.

World Health Organization. (2009b). *WHO guidelines on hand hygiene in healthcare:a summary*. Retrieved from www.who.int

World Health Organization. (2011). *WHO Statistical Information System (WHOSIS)*. Retrieved from https://www.who.int/whosis/whostat/2011/en

World Health Organization. (2013). *MRSA infection*. Retrieved February 8, 2019, from https://www.who.int/patientsafety/patients_for_patient/PFPS-webinar1_203.pdf

World Health Organization. (2014a). *Antimicrobial resistance: Global report on surveillance*. Retrieved from www.who.intwww.who.int

World Health Organization. (2014b). *Antimicrobial resistance: Global report on surveillance.* . Retrieved July 30, 2018, from www.who.int

World Health Organization. (2014c). *Antimicrobial resistance:Global report on surveillance*. Retrieved April 4, 2018, from www.wpro.who.int

World Health Organization. (2014d). *Antimicrobial resistance:Global report on surveillance*. Retrieved from www.who.int

World Health Organization. (2015). *Global Health Observatory (GHO) data*. Retrieved from https://www.who.int/gho/countries/en/

World Health Organization. (2016). *National actions for global change on antimicrobial resistance*. Retrieved October 1, 2018, from iris.wpro.who.int

World Health Organization. (2018). *Antimicrobial resistance*. Retrieved from https://www.who.int/antimicrobial-resistance/en/

World Health Organization (WHO). (2011). *World Health Statistics 2011*. Retrieved from https://www.who.int

Yochay, G. R., Rubinstein, E., Barzilai, A., Cameli.Y, Kuint, J., Etienne, J., . . . Keller, N. (2005). MRSA in neonatal intensive care unit. *Emerging Infectious Diseases, 11*(3), 453-456.

York, M. K., Gibbs, L., Chehab, F., & Brooks, G. F. (1996). Comparison of PCR detection of mecA with standard susceptibility testing methods to determine methicillin

resistant in Coagulase-Negative *StaphylococciJournal of Clinical Microbiology*, 249-253.

# Glossary

**Aetiology:** the study of the causes of disease.

**Antibiotic:** a medicine that inhibits the growth or destroys micro-organisms.

**Antimicrobial:** an agent that kills micro-organisms or stops their growth.

**Bacteriostatic:** a biological or chemical agent that prevents bacteria from reproducing, whilst not killing them completely.

**Beta-lactams:** a class of broad-spectrum antibiotics consisting of all antibiotic agents that contain a beta-lactam ring in their molecular structures. These antibiotics include penicillin derivatives, cephalosporins, monobactams and carbapenems.

**Colonisation:** having micro-organisms in or on the body without becoming sick.

**Epidemiology:** the branch of medicine that deals with the incidence, distribution and possible causes of diseases and other factors relating to health.

**Epistemology:** the theory of knowledge, especially with regards to its methods, validity and scope and the distinction between justified belief and opinion.

**Hospital-acquired infection(HAI):** an infection that someone acquires while under medical care.It has not been present before in that individual.

**Infection:** The invasion and multiplication of micro-organisms such as bacteria, viruses and parasites that are not normally present within the body.

**Morbidity:** the condition of being diseased.

**Mortality:** the state of being subject to death.

**Pathogenesis:** the manner of development of a disease.

**Pharmacodynamics:** the branch of pharmacology concerned with the effects of drugs and the mechanism of their actions.

**Pharmacokinetics:** the branch of pharmacology concerned with the movement of drugs within the body.

**Pharmacology:** the branch of medicine concerned with the uses, effects and modes of actions of drugs.

**Polymerase chain reaction (PCR):** a method of making multiple copies of a DNA sequence, involving repeated actions with a polymerase.

**Positivism:**

**Prevalence:** a measure of all individuals affected by a disease at a particular time.

**Susceptibility:** the tendency to be affected by something.

**Toxin:** a biologically produced poison by bacteria.

**Toxinosis:** pathogenesis caused by a bacteria toxin.

**Virulence:** a pathogen's or a microbe's ability to infect or damage a host.

# Appendix A:AUTEC approval letter

JedMontayre

Faculty of Health and Environmental Sciences

Dear Jed

Ethics Application: 18/112**Antimicrobial susceptibility profile of Methicillin-resistant Staphylococcus aureus (MRSA) in Port Moresby General Hospital, Papua New Guinea. A retrospective study**

I wish to advise you that the Auckland University of Technology Ethics Committee (AUTEC) has **approved** your ethics application at its meeting of 19 March 2018.

This approval is for three years, expiring 19 March 2021.

**Standard Conditions of Approval**

1. A progress report is due annually on the anniversary of the approval date, using form EA2, which is available online through http://www.aut.ac.nz/researchethics.
2. A final report is due at the expiration of the approval period, or, upon completion of project, using form EA3, which is available online through http://www.aut.ac.nz/researchethics.
3. Any amendments to the project must be approved by AUTEC prior to being implemented. Amendments can be requested using the EA2 form:http://www.aut.ac.nz/researchethics.
4. Any serious or unexpected adverse events must be reported to AUTEC Secretariat as a matter of priority.
5. Any unforeseen events that might affect continued ethical acceptability of the project should also be reported to the AUTEC Secretariat as a matter of priority.

Please quote the application number and title on all future correspondence related to this project.

AUTEC grants ethical approval only. If you require management approval for access for your research from another institution or organisation, then you are responsible for obtaining it. If the research is undertaken outside New Zealand, you need to meet all locality legal and ethical obligations and requirements. You are reminded that it is your responsibility to ensure that the spelling and grammar of documents being provided to participants or external organisations is of a high standard.

For any enquiries please contact ethics@aut.ac.nz

Yours sincerely,

Kate O'Connor

Executive Manager

**Auckland University of Technology Ethics Committee**

Cc: jmpamu@gmail.com; Eleanor Holroyd

# Appendix B: Port Moresby General Hospital approval letter

From: Jamie Pamu <jmpamu@gmail.com>
Sent: Friday, 23 March 2018 9:29 AM
To: david_mokela@pomgen.gov.pg
Subject: Seeking permission to collect data for research

Greetings Dr Mokela.

As per the above I would seek the management's permission to obtain data at the Microbiology laboratory in Port Moresby General Hospital as a pre-requisite to completing Master of Health Science at the Auckland University of Technology in New Zealand.

Attached is my approved proposal from the Auckland University of Technology.I wish to commence data collection next Month,April,2018.

Your permission will be greatly appreciated.

Kind regards!
Jamblyne Pamu

---

From: david_mokela@pomgen.gov.pg
Sent: Monday, 26 March 2018 5:20 PM
To: Phillip, uarageroa, me
Subject: Re: Seeking permission to collect data for research

Dear Ms Jamblyne Pamu,

Approval is hereby granted for to have access to Microbiology Laboratory data solely for the purpose as requested.

Thank you

---

From: Jamie Pamu <jmpamu@gmail.com>
Sent: Monday, 26 March 2018 6:08 PM
To: Dr, Phillip, Ua
Subject: Re: Seeking permission to collect data for research

Thank you very much.

Kindest Regards!
Jamblyne Pamu

# Appendix C: Sensitive data safety management protocol

**Auckland University of Technology Ethics Committee (AUTEC).**

**Sensitive Data Safety Management Protocol**

**Project title and brief Description**

Antimicrobial and susceptibility pattern of Methicillin-resistant *Staphylococcus aureus* in Port Moresby general hospital, Papua New Guinea (PNG). A retrospective study.

This research will document the prevalence and susceptibility pattern of methicillin-resistant *Staphylococcus aureus* at the Port Moresby general hospital in Papua New Guinea. Determining methicillin resistant *Staphylococcus aureus* prevalence and susceptibility pattern will enable clinicians to properly treat patients with appropriate antibiotics and reduce risk of the emergence of methicillin-resistant *Staphylococcus aureus* (CDC,2013). There is increased risk of infection, mortality and morbidity associated with methicillin-resistant *Staphylococcus aureus*. In a country such as Papua New Guinea, the burden of disease is high and costs associated with health are expandable.

This study will be a retrospective study, collecting data from registry books and from the database of the different specimen sent in for suspected *Staph. aureus* cases for Microscopy, Culture and Sensitivity (MCS) and were analysed prospectively. The study will gather data from patients (baby to adults) with confirmed methicillin-resistant *Staphylococcus aureus* isolates over a five-year period from, 2011-2016. The results from this study will help clinicians treat patients infected with methicillin-resistant *Staphylococcus aureus* with correct antibiotics, will help the hospital with its infection control policy and reduce the economic burden of healthcare-associated infections caused by methicillin-resistant *Staphylococcus aureus* in Port Moresby general hospital.

**Primary Researcher**

Jamblyne Pamu

**Supervisors**

Dr Jed Montayre

Professor Eleanor Holroyd

**Production of data**

- Identifiable medical records will be produced.

Data will be collected using a structured self-prepared template (MS Excel).Identifiable data will first be decoded and stored in a password protected file. *Identifiable variables will be aggregated, and their precision reduced.*

- There will be sufficient storage space on laptop, an external drive and Google's one drive for storage of data.
- *The estimated data generated will presumably be less than 500 megabytes. There will be sufficient storage on my laptop as well as an external drive which has 1 terabyte space. Data will be stored on Google's one drive.*
- *Data will also be stored on one drive as a back-up.*
- *Date generated from the field will be stored to University storage right after data collection completion and will occur upon returning to Auckland in July 2018.*

- *A file naming convention will be used. (For example, different specimen will be entered as xx and the years that they were recorded will be entered as YYYY.*
- *Quality of data will be checked daily after data entry. The data will be backed up daily as well and stored on an external drive. Access rights to data will be limited to the researcher and the supervisors only.*

*Ethical requirements for the data*

- *The data is sensitive because it contains identifiable information such as patient's names and age.*
- *Physical data (names of patients) will be collected in Port Moresby General Hospital in Papua New Guinea. Data will be decoded and entered Excel worksheet in PNG.Digital data from data base has names of patients omitted.*
- *Data will be made anonymous by leaving out patient's names and giving code numbers. Other identifying variables are part of the research (for example age and wards where the patients were admitted)*
- *My sponsor (MFAT) do not have specific data sharing and managing requirements.*
- *Data will be embargoed and destroyed after 10 years as per AUTEC guideline for storage and destruction of health-related data.*
- *There are no participants in this research, they will not consent, however the hospital will be informed.*

*Plans for data sharing and access*

- *Data will be shared with the supervisors as per our discussion.*
- *Research involves information about people, the hospital will be informed prior to data collection.*
- *Data will not be released immediately, it will be embargoed.*
- *Data will have restrictions and will only be available to the supervisors and biostaticians at AUT.*
- *Data will only be available only for the purpose it is intended for, after analysis data will be locked and stored away for a period of 10 years as per AUTEC guidelines for storage of health data (18.4.2). No data repository will be used.*

*Main data challenges*

- *The main challenge that is foreseen currently is data analysis using statistical techniques. Biostaticians are available at AUT for assistance.*
- *The policies for ethics at AUT(AUTEC) guidelines and procedures regarding research have been read and understood.*
- *Data will be managed by the primary supervisor and stored in three locations (ipad, external drive and Goggle's one drive)*
- *The primary researcher will be responsible for the storage of data while data collection is going on. The Faculty of Health and Environmental Science will be responsible for the storage of data after completion as per AUTEC guidelines for the storage of data.*
- *The data will be managed by the primary researcher and stored in three locations (external drive, one drive and an ipad).*
- *Currently there are sufficient resources available to deliver this plan.*
- *The data will be destroyed if the primary research leaves mid project.*

# Appendix D: Codebook for SPSS

Records 1-1000

**Code:**
PUS- 1
SPM- 2
VB-3
ASP/BODY FLUIDS-4
UR=5
BACTEC=6

**Month:**
201201= 1
201202 =2
201203= 3
201204= 4
201205= 5
201206=6
201207= 7
201208=8
201209=9
201210=10
201211=11
201212=12
201301= 13
201302=14
201303=15
201304=16
201305=17
201306=18
201307=19
201308=20
201309=21
201310=22
201311=23
201312=24
201401=25
201402=26
201403=27
201404=28
201405=29
201406=30
201407=31
201408=32
201409=33
201410=34
201411=35
201412=36
201501=37
201502=38
201503=39
201504=40
201505=41
201506=42
201507=43
201508=44
201509=45
201510=46
201511=47
201512=48
201601=49
201602=50
201603=51
201604=52
201605=53
201606=54
201607=55
201608=56
201609=57
201610=58
201611=59
201612=60

**Age (years)**
0-4=1
5-10=2
11-15=3
16-20=4
21-25=5
26-30=6
31-35=7
36-40=8
41-45=9
46-50=10
51-55=11
56-60=12
61-65=13
66-70=14
71-75=15
76-80=16
81-85=17
86-90=18
91-95=19
96-100=20

**Age group**
00-04=1
05-10=2
11-15=3
16-20=4
20+=5
LE 1month=6
LE 1 year=7
No age recorded=8

**Sex**
Gender not recorded=0
Male=1
Female=2

**Ward types**
ICU=1
AOPD=10
GOPD=11
ANC=12
SOPD=13
TBC=14
PRIVATE=15
OTHER=16
OUTSIDE=17
Medical=2
Surgical=3
Paeds=4
SCN=5
COPD=6
Emergency dept=7
O&G=8
Specialist clinics=9
Labour ward=19
No ward recorded=18

**SPECIMEN**
SWABS=1
CATHETER TIPS=2
SPM=3
URINE=4
BLOOD=5
ASPIRATES/BODY FLUIDS=6
CSF=7
ANTIBACTERIALS
CS=1
CSR=2
Not done=0
ES=3
ER=4
SXTS=5
SXTR=6
VAS=7
VAR=8
TES=9
TER=10
FOXS=1
FOXR=2

# Appendix E: Example of the original data collection sheet

| CODE | YEAR | AGE RANGE (YRS) | SEX | WARD | SPECIMEN TYPE | CLINICAL NOTES | CONFIRMED MRSA (YES/NO) | C (S/R) | E(S/R) | SXT (S/R) | VA (S/R) | TE(S/R) | FOX/OX |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | | | | | | | | | | | | | |

# Appendix F: Results of crosstabulation of gender vs. antibacterials (SPSS output)

**Gender Vs. Chloramphenicol (30µg)**

**Case Processing Summary**

| | Cases | | | | | |
|---|---|---|---|---|---|---|
| | Valid | | Missing | | Total | |
| | N | Percent | N | Percent | N | Percent |
| SEX * C 30ug | 1006 | 100.0% | 0 | 0.0% | 1006 | 100.0% |
| SEX * E 15 ug | 1006 | 100.0% | 0 | 0.0% | 1006 | 100.0% |
| SEX * SXT 25ug | 1006 | 100.0% | 0 | 0.0% | 1006 | 100.0% |
| SEX * VA 30ug | 1006 | 100.0% | 0 | 0.0% | 1006 | 100.0% |
| SEX * TE 30ug | 1006 | 100.0% | 0 | 0.0% | 1006 | 100.0% |

**Crosstab**

| | | | C 30ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | CS | CR | Total |
| SEX | No sex recorded | Count | 0 | 3 | 0 | 3 |
| | | % within SEX | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within C 30ug | 0.0% | 0.4% | 0.0% | 0.3% |
| | | % of Total | 0.0% | 0.3% | 0.0% | 0.3% |
| | Male | Count | 7 | 402 | 120 | 529 |
| | | % within SEX | 1.3% | 76.0% | 22.7% | 100.0% |
| | | % within C 30ug | 100.0% | 50.5% | 59.1% | 52.6% |
| | | % of Total | 0.7% | 40.0% | 11.9% | 52.6% |
| | Female | Count | 0 | 391 | 83 | 474 |
| | | % within SEX | 0.0% | 82.5% | 17.5% | 100.0% |
| | | % within C 30ug | 0.0% | 49.1% | 40.9% | 47.1% |
| | | % of Total | 0.0% | 38.9% | 8.3% | 47.1% |
| Total | | Count | 7 | 796 | 203 | 1006 |
| | | % within SEX | 0.7% | 79.1% | 20.2% | 100.0% |
| | | % within C 30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 0.7% | 79.1% | 20.2% | 100.0% |

**Chi-Square Tests**

| | Value | df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 11.735[a] | 4 | .019 |
| Likelihood Ratio | 15.028 | 4 | .005 |
| N of Valid Cases | 1006 | | |

a. 5 cells (55.6%) have expected count less than 5. The minimum expected count is .02.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .108 | .019 |
| | Cramer's V | .076 | .019 |
| N of Valid Cases | | 1006 | |

## Gender Vs. Septrin (25µg)

**Crosstab**

| | | | SXTND | SXT 25ug SXTS | SXTR | Total |
|---|---|---|---|---|---|---|
| SEX | No sex recorded | Count | 0 | 3 | 0 | 3 |
| | | % within SEX | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within SXT 25ug | 0.0% | 0.5% | 0.0% | 0.3% |
| | | % of Total | 0.0% | 0.3% | 0.0% | 0.3% |
| | Male | Count | 184 | 304 | 41 | 529 |
| | | % within SEX | 34.8% | 57.5% | 7.8% | 100.0% |
| | | % within SXT 25ug | 54.8% | 50.0% | 66.1% | 52.6% |
| | | % of Total | 18.3% | 30.2% | 4.1% | 52.6% |
| | Female | Count | 152 | 301 | 21 | 474 |
| | | % within SEX | 32.1% | 63.5% | 4.4% | 100.0% |
| | | % within SXT 25ug | 45.2% | 49.5% | 33.9% | 47.1% |
| | | % of Total | 15.1% | 29.9% | 2.1% | 47.1% |
| Total | | Count | 336 | 608 | 62 | 1006 |
| | | % within SEX | 33.4% | 60.4% | 6.2% | 100.0% |
| | | % within SXT 25ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 33.4% | 60.4% | 6.2% | 100.0% |

**Chi-Square Tests**

| | Value | df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 8.499[a] | 4 | .075 |
| Likelihood Ratio | 9.645 | 4 | .047 |
| N of Valid Cases | 1006 | | |

a. 3 cells (33.3%) have expected count less than 5. The minimum expected count is .18.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .092 | .075 |
| | Cramer's V | .065 | .075 |
| N of Valid Cases | | 1006 | |

**Gender Vs. Vancomycin (30µg)**

**Crosstab**

| | | | VA 30ug | | | | |
|---|---|---|---|---|---|---|---|
| | | | VAND | VAS | VAR | R | Total |
| SEX | No sex recorded | Count | 0 | 3 | 0 | 0 | 3 |
| | | % within SEX | 0.0% | 100.0% | 0.0% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 0.3% | 0.0% | 0.0% | 0.3% |
| | | % of Total | 0.0% | 0.3% | 0.0% | 0.0% | 0.3% |
| | Male | Count | 4 | 503 | 22 | 0 | 529 |
| | | % within SEX | 0.8% | 95.1% | 4.2% | 0.0% | 100.0% |
| | | % within VA 30ug | 80.0% | 52.3% | 56.4% | 0.0% | 52.6% |
| | | % of Total | 0.4% | 50.0% | 2.2% | 0.0% | 52.6% |
| | Female | Count | 1 | 455 | 17 | 1 | 474 |
| | | % within SEX | 0.2% | 96.0% | 3.6% | 0.2% | 100.0% |
| | | % within VA 30ug | 20.0% | 47.3% | 43.6% | 100.0% | 47.1% |
| | | % of Total | 0.1% | 45.2% | 1.7% | 0.1% | 47.1% |
| Total | | Count | 5 | 961 | 39 | 1 | 1006 |
| | | % within SEX | 0.5% | 95.5% | 3.9% | 0.1% | 100.0% |
| | | % within VA 30ug | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 0.5% | 95.5% | 3.9% | 0.1% | 100.0% |

**Chi-Square Tests**

| | Value | df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 2.988[a] | 6 | .810 |
| Likelihood Ratio | 3.620 | 6 | .728 |
| N of Valid Cases | 1006 | | |

a. 8 cells (66.7%) have expected count less than 5. The minimum expected count is .00.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .054 | .810 |
| | Cramer's V | .039 | .810 |
| N of Valid Cases | | 1006 | |

**Gender Vs.Tetracyline (30µg)**

**Crosstab**

| | | | TE 30ug | | | |
|---|---|---|---|---|---|---|
| | | | TEND | TER | TES | Total |
| SEX | No sex recorded | Count | 0 | 1 | 2 | 3 |
| | | % within SEX | 0.0% | 33.3% | 66.7% | 100.0% |
| | | % within TE 30ug | 0.0% | 1.6% | 0.2% | 0.3% |
| | | % of Total | 0.0% | 0.1% | 0.2% | 0.3% |
| | Male | Count | 6 | 35 | 488 | 529 |
| | | % within SEX | 1.1% | 6.6% | 92.2% | 100.0% |
| | | % within TE 30ug | 50.0% | 57.4% | 52.3% | 52.6% |
| | | % of Total | 0.6% | 3.5% | 48.5% | 52.6% |
| | Female | Count | 6 | 25 | 443 | 474 |
| | | % within SEX | 1.3% | 5.3% | 93.5% | 100.0% |
| | | % within TE 30ug | 50.0% | 41.0% | 47.5% | 47.1% |
| | | % of Total | 0.6% | 2.5% | 44.0% | 47.1% |
| Total | | Count | 12 | 61 | 933 | 1006 |
| | | % within SEX | 1.2% | 6.1% | 92.7% | 100.0% |
| | | % within TE 30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 1.2% | 6.1% | 92.7% | 100.0% |

**Chi-Square Tests**

| | Value | df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 4.765[a] | 4 | .312 |
| Likelihood Ratio | 2.933 | 4 | .569 |
| N of Valid Cases | 1006 | | |

a. 3 cells (33.3%) have expected count less than 5. The minimum expected count is .04.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .069 | .312 |
| | Cramer's V | .049 | .312 |
| N of Valid Cases | | 1006 | |

# Appendix G: Results of crosstabulation of clinical infections vs. antibacterials (SPSS output)

**Clinical infection Vs. Chloramphenicol (30µg)**

**Crosstab**

| | | | CHLORAMPHENICOL 30ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | R | S | Total |
| Clinical notes group 2 | Blood | Count | 1 | 27 | 104 | 132 |
| | | % within Clinical notes group 2 | 0.8% | 20.5% | 78.8% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 14.3% | 13.0% | 13.1% | 13.1% |
| | | % of Total | 0.1% | 2.7% | 10.3% | 13.1% |
| | Bone | Count | 0 | 10 | 38 | 48 |
| | | % within Clinical notes group 2 | 0.0% | 20.8% | 79.2% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 0.0% | 4.8% | 4.8% | 4.8% |
| | | % of Total | 0.0% | 1.0% | 3.8% | 4.8% |
| | Central Nervous system | Count | 0 | 3 | 8 | 11 |
| | | % within Clinical notes group 2 | 0.0% | 27.3% | 72.7% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 0.0% | 1.4% | 1.0% | 1.1% |
| | | % of Total | 0.0% | 0.3% | 0.8% | 1.1% |
| | Clinical details missing | Count | 1 | 28 | 151 | 180 |
| | | % within Clinical notes group 2 | 0.6% | 15.6% | 83.9% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 14.3% | 13.5% | 19.1% | 17.9% |
| | | % of Total | 0.1% | 2.8% | 15.0% | 17.9% |
| | DM | Count | 0 | 5 | 29 | 34 |
| | | % within Clinical notes group 2 | 0.0% | 14.7% | 85.3% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 0.0% | 2.4% | 3.7% | 3.4% |
| | | % of Total | 0.0% | 0.5% | 2.9% | 3.4% |
| | Joints | Count | 0 | 0 | 8 | 8 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % within CHLORAMPHENICOL 30ug | 0.0% | 0.0% | 1.0% | 0.8% |
| | | % of Total | 0.0% | 0.0% | 0.8% | 0.8% |
| | Others | Count | 0 | 12 | 32 | 44 |
| | | % within Clinical notes group 2 | 0.0% | 27.3% | 72.7% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 0.0% | 5.8% | 4.0% | 4.4% |
| | | % of Total | 0.0% | 1.2% | 3.2% | 4.4% |
| | Respiratory system | Count | 2 | 18 | 49 | 69 |
| | | % within Clinical notes group 2 | 2.9% | 26.1% | 71.0% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 28.6% | 8.7% | 6.2% | 6.9% |
| | | % of Total | 0.2% | 1.8% | 4.9% | 6.9% |
| | Skin | Count | 3 | 99 | 357 | 459 |
| | | % within Clinical notes group 2 | 0.7% | 21.6% | 77.8% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 42.9% | 47.8% | 45.1% | 45.6% |
| | | % of Total | 0.3% | 9.8% | 35.5% | 45.6% |
| | Urinary Tract | Count | 0 | 5 | 16 | 21 |
| | | % within Clinical notes group 2 | 0.0% | 23.8% | 76.2% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 0.0% | 2.4% | 2.0% | 2.1% |
| | | % of Total | 0.0% | 0.5% | 1.6% | 2.1% |
| Total | | Count | 7 | 207 | 792 | 1006 |
| | | % within Clinical notes group 2 | 0.7% | 20.6% | 78.7% | 100.0% |
| | | % within CHLORAMPHENICOL 30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 0.7% | 20.6% | 78.7% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 15.102[a] | 18 | .655 |
| Likelihood Ratio | 15.801 | 18 | .606 |
| N of Valid Cases | 1006 | | |

a. 13 cells (43.3%) have expected count less than 5. The minimum expected count is .06.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .123 | .655 |
| | Cramer's V | .087 | .655 |
| | Contingency Coefficient | .122 | .655 |
| N of Valid Cases | | 1006 | |

## Clinical infections Vs. Erythromycin

**Crosstab**

| | | | ERYTHROMYCIN E 15 ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | R | S | Total |
| Clinical notes group 2 | Blood | Count | 6 | 36 | 90 | 132 |
| | | % within Clinical notes group 2 | 4.5% | 27.3% | 68.2% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 11.3% | 13.2% | 13.2% | 13.1% |
| | | % of Total | 0.6% | 3.6% | 8.9% | 13.1% |
| | Bone | Count | 5 | 10 | 33 | 48 |
| | | % within Clinical notes group 2 | 10.4% | 20.8% | 68.8% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 9.4% | 3.7% | 4.9% | 4.8% |
| | | % of Total | 0.5% | 1.0% | 3.3% | 4.8% |
| | Central Nervous system | Count | 0 | 4 | 7 | 11 |
| | | % within Clinical notes group 2 | 0.0% | 36.4% | 63.6% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 0.0% | 1.5% | 1.0% | 1.1% |
| | | % of Total | 0.0% | 0.4% | 0.7% | 1.1% |
| | Clinical details missing | Count | 1 | 45 | 134 | 180 |
| | | % within Clinical notes group 2 | 0.6% | 25.0% | 74.4% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 1.9% | 16.5% | 19.7% | 17.9% |
| | | % of Total | 0.1% | 4.5% | 13.3% | 17.9% |
| | DM | Count | 2 | 6 | 26 | 34 |
| | | % within Clinical notes group 2 | 5.9% | 17.6% | 76.5% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 3.8% | 2.2% | 3.8% | 3.4% |
| | | % of Total | 0.2% | 0.6% | 2.6% | 3.4% |
| | Joints | Count | 0 | 0 | 8 | 8 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 0.0% | 0.0% | 1.2% | 0.8% |
| | | % of Total | 0.0% | 0.0% | 0.8% | 0.8% |
| | Others | Count | 3 | 19 | 22 | 44 |
| | | % within Clinical notes group 2 | 6.8% | 43.2% | 50.0% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 5.7% | 7.0% | 3.2% | 4.4% |
| | | % of Total | 0.3% | 1.9% | 2.2% | 4.4% |
| | Respiratory system | Count | 0 | 21 | 48 | 69 |
| | | % within Clinical notes group 2 | 0.0% | 30.4% | 69.6% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 0.0% | 7.7% | 7.1% | 6.9% |
| | | % of Total | 0.0% | 2.1% | 4.8% | 6.9% |
| | Skin | Count | 36 | 126 | 297 | 459 |
| | | % within Clinical notes group 2 | 7.8% | 27.5% | 64.7% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 67.9% | 46.2% | 43.7% | 45.6% |
| | | % of Total | 3.6% | 12.5% | 29.5% | 45.6% |
| | Urinary Tract | Count | 0 | 6 | 15 | 21 |
| | | % within Clinical notes group 2 | 0.0% | 28.6% | 71.4% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 0.0% | 2.2% | 2.2% | 2.1% |
| | | % of Total | 0.0% | 0.6% | 1.5% | 2.1% |
| Total | | Count | 53 | 273 | 680 | 1006 |
| | | % within Clinical notes group 2 | 5.3% | 27.1% | 67.6% | 100.0% |
| | | % within ERYTHROMYCIN E 15 ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 5.3% | 27.1% | 67.6% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 36.609[a] | 18 | .006 |
| Likelihood Ratio | 47.623 | 18 | .000 |
| N of Valid Cases | 1006 | | |

a. 9 cells (30.0%) have expected count less than 5. The minimum expected count is .42.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .191 | .006 |
| | Cramer's V | .135 | .006 |
| | Contingency Coefficient | .187 | .006 |
| N of Valid Cases | | 1006 | |

## Clinical infections Vs. Septrin (25µg)

**Crosstab**

| | | | SEPTRIN (SXT)25ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | R | S | Total |
| Clinical notes group 2 | Blood | Count | 50 | 10 | 72 | 132 |
| | | % within Clinical notes group 2 | 37.9% | 7.6% | 54.5% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 14.9% | 16.1% | 11.8% | 13.1% |
| | | % of Total | 5.0% | 1.0% | 7.2% | 13.1% |
| | Bone | Count | 22 | 2 | 24 | 48 |
| | | % within Clinical notes group 2 | 45.8% | 4.2% | 50.0% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 6.5% | 3.2% | 3.9% | 4.8% |
| | | % of Total | 2.2% | 0.2% | 2.4% | 4.8% |
| | Central Nervous system | Count | 5 | 2 | 4 | 11 |
| | | % within Clinical notes group 2 | 45.5% | 18.2% | 36.4% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 1.5% | 3.2% | 0.7% | 1.1% |
| | | % of Total | 0.5% | 0.2% | 0.4% | 1.1% |
| | Clinical details missing | Count | 34 | 13 | 133 | 180 |
| | | % within Clinical notes group 2 | 18.9% | 7.2% | 73.9% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 10.1% | 21.0% | 21.9% | 17.9% |
| | | % of Total | 3.4% | 1.3% | 13.2% | 17.9% |
| | DM | Count | 12 | 1 | 21 | 34 |
| | | % within Clinical notes group 2 | 35.3% | 2.9% | 61.8% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 3.6% | 1.6% | 3.5% | 3.4% |
| | | % of Total | 1.2% | 0.1% | 2.1% | 3.4% |
| | Joints | Count | 0 | 0 | 8 | 8 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 0.0% | 0.0% | 1.3% | 0.8% |
| | | % of Total | 0.0% | 0.0% | 0.8% | 0.8% |
| | Others | Count | 14 | 5 | 25 | 44 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % within Clinical notes group 2 | 31.8% | 11.4% | 56.8% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 4.2% | 8.1% | 4.1% | 4.4% |
| | | % of Total | 1.4% | 0.5% | 2.5% | 4.4% |
| | Respiratory system | Count | 29 | 5 | 35 | 69 |
| | | % within Clinical notes group 2 | 42.0% | 7.2% | 50.7% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 8.6% | 8.1% | 5.8% | 6.9% |
| | | % of Total | 2.9% | 0.5% | 3.5% | 6.9% |
| | Skin | Count | 156 | 21 | 282 | 459 |
| | | % within Clinical notes group 2 | 34.0% | 4.6% | 61.4% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 46.4% | 33.9% | 46.4% | 45.6% |
| | | % of Total | 15.5% | 2.1% | 28.0% | 45.6% |
| | Urinary Tract | Count | 14 | 3 | 4 | 21 |
| | | % within Clinical notes group 2 | 66.7% | 14.3% | 19.0% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 4.2% | 4.8% | 0.7% | 2.1% |
| | | % of Total | 1.4% | 0.3% | 0.4% | 2.1% |
| Total | | Count | 336 | 62 | 608 | 1006 |
| | | % within Clinical notes group 2 | 33.4% | 6.2% | 60.4% | 100.0% |
| | | % within SEPTRIN (SXT)25ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 33.4% | 6.2% | 60.4% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 54.374[a] | 18 | .001 |
| Likelihood Ratio | 57.882 | 18 | .001 |
| N of Valid Cases | 1006 | | |

a. 10 cells (33.3%) have expected count less than 5. The minimum expected count is .49.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .232 | .000 |
| | Cramer's V | .164 | .000 |
| | Contingency Coefficient | .226 | .000 |
| N of Valid Cases | | 1006 | |

**Clinical infections Vs. Vancomycin (30µg)**

**Crosstab**

| | | | VANCOMYCIN (VA) 30ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | R | S | Total |
| Clinical notes group 2 | Blood | Count | 0 | 4 | 128 | 132 |
| | | % within Clinical notes group 2 | 0.0% | 3.0% | 97.0% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 10.3% | 13.3% | 13.1% |
| | | % of Total | 0.0% | 0.4% | 12.7% | 13.1% |
| | Bone | Count | 0 | 3 | 45 | 48 |
| | | % within Clinical notes group 2 | 0.0% | 6.3% | 93.8% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 7.7% | 4.7% | 4.8% |
| | | % of Total | 0.0% | 0.3% | 4.5% | 4.8% |
| | Central Nervous system | Count | 0 | 0 | 11 | 11 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 0.0% | 1.1% | 1.1% |
| | | % of Total | 0.0% | 0.0% | 1.1% | 1.1% |
| | Clinical details missing | Count | 1 | 6 | 173 | 180 |
| | | % within Clinical notes group 2 | 0.6% | 3.3% | 96.1% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 20.0% | 15.4% | 18.0% | 17.9% |
| | | % of Total | 0.1% | 0.6% | 17.2% | 17.9% |
| | DM | Count | 0 | 0 | 34 | 34 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 0.0% | 3.5% | 3.4% |
| | | % of Total | 0.0% | 0.0% | 3.4% | 3.4% |
| | Joints | Count | 0 | 0 | 8 | 8 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 0.0% | 0.8% | 0.8% |
| | | % of Total | 0.0% | 0.0% | 0.8% | 0.8% |
| | Others | Count | 0 | 6 | 38 | 44 |
| | | % within Clinical notes group 2 | 0.0% | 13.6% | 86.4% | 100.0% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 15.4% | 4.0% | 4.4% |
| | | % of Total | 0.0% | 0.6% | 3.8% | 4.4% |
| | Respiratory system | Count | 1 | 1 | 67 | 69 |
| | | % within Clinical notes group 2 | 1.4% | 1.4% | 97.1% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 20.0% | 2.6% | 7.0% | 6.9% |
| | | % of Total | 0.1% | 0.1% | 6.7% | 6.9% |
| | Skin | Count | 3 | 17 | 439 | 459 |
| | | % within Clinical notes group 2 | 0.7% | 3.7% | 95.6% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 60.0% | 43.6% | 45.6% | 45.6% |
| | | % of Total | 0.3% | 1.7% | 43.6% | 45.6% |
| | Urinary Tract | Count | 0 | 2 | 19 | 21 |
| | | % within Clinical notes group 2 | 0.0% | 9.5% | 90.5% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 0.0% | 5.1% | 2.0% | 2.1% |
| | | % of Total | 0.0% | 0.2% | 1.9% | 2.1% |
| Total | | Count | 5 | 39 | 962 | 1006 |
| | | % within Clinical notes group 2 | 0.5% | 3.9% | 95.6% | 100.0% |
| | | % within VANCOMYCIN (VA) 30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 0.5% | 3.9% | 95.6% | 100.0% |

Chi-Square Tests

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 20.356[a] | 18 | .313 |
| Likelihood Ratio | 18.891 | 18 | .399 |
| N of Valid Cases | 1006 | | |

a. 17 cells (56.7%) have expected count less than 5. The minimum expected count is .04.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .142 | .313 |
| | Cramer's V | .101 | .313 |
| | Contingency Coefficient | .141 | .313 |
| N of Valid Cases | | 1006 | |

**Clinical infections Vs. Tetracycline (30µg)**

**Crosstab**

| | | | TETRACYCLINE (TE)30ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | R | S | Total |
| Clinical notes group 2 | Blood | Count | 4 | 8 | 120 | 132 |
| | | % within Clinical notes group 2 | 3.0% | 6.1% | 90.9% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 33.3% | 12.7% | 12.9% | 13.1% |
| | | % of Total | 0.4% | 0.8% | 11.9% | 13.1% |
| | Bone | Count | 0 | 2 | 46 | 48 |
| | | % within Clinical notes group 2 | 0.0% | 4.2% | 95.8% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 0.0% | 3.2% | 4.9% | 4.8% |
| | | % of Total | 0.0% | 0.2% | 4.6% | 4.8% |
| | Central Nervous system | Count | 0 | 0 | 11 | 11 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 0.0% | 0.0% | 1.2% | 1.1% |
| | | % of Total | 0.0% | 0.0% | 1.1% | 1.1% |
| | Clinical details missing | Count | 2 | 10 | 168 | 180 |
| | | % within Clinical notes group 2 | 1.1% | 5.6% | 93.3% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 16.7% | 15.9% | 18.0% | 17.9% |
| | | % of Total | 0.2% | 1.0% | 16.7% | 17.9% |
| | DM | Count | 0 | 1 | 33 | 34 |
| | | % within Clinical notes group 2 | 0.0% | 2.9% | 97.1% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 0.0% | 1.6% | 3.5% | 3.4% |
| | | % of Total | 0.0% | 0.1% | 3.3% | 3.4% |
| | Joints | Count | 0 | 0 | 8 | 8 |
| | | % within Clinical notes group 2 | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 0.0% | 0.0% | 0.9% | 0.8% |
| | | % of Total | 0.0% | 0.0% | 0.8% | 0.8% |
| | Others | Count | 1 | 7 | 36 | 44 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % within Clinical notes group 2 | 2.3% | 15.9% | 81.8% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 8.3% | 11.1% | 3.9% | 4.4% |
| | | % of Total | 0.1% | 0.7% | 3.6% | 4.4% |
| | Respiratory system | Count | 0 | 3 | 66 | 69 |
| | | % within Clinical notes group 2 | 0.0% | 4.3% | 95.7% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 0.0% | 4.8% | 7.1% | 6.9% |
| | | % of Total | 0.0% | 0.3% | 6.6% | 6.9% |
| | Skin | Count | 5 | 28 | 426 | 459 |
| | | % within Clinical notes group 2 | 1.1% | 6.1% | 92.8% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 41.7% | 44.4% | 45.8% | 45.6% |
| | | % of Total | 0.5% | 2.8% | 42.3% | 45.6% |
| | Urinary Tract | Count | 0 | 4 | 17 | 21 |
| | | % within Clinical notes group 2 | 0.0% | 19.0% | 81.0% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 0.0% | 6.3% | 1.8% | 2.1% |
| | | % of Total | 0.0% | 0.4% | 1.7% | 2.1% |
| Total | | Count | 12 | 63 | 931 | 1006 |
| | | % within Clinical notes group 2 | 1.2% | 6.3% | 92.5% | 100.0% |
| | | % within TETRACYCLINE (TE)30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 1.2% | 6.3% | 92.5% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 22.439[a] | 18 | .213 |
| Likelihood Ratio | 21.041 | 18 | .277 |
| N of Valid Cases | 1006 | | |

a. 16 cells (53.3%) have expected count less than 5. The minimum expected count is .10.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .149 | .213 |
| | Cramer's V | .106 | .213 |
| | Contingency Coefficient | .148 | .213 |
| N of Valid Cases | | 1006 | |

# Appendix H: Results of crosstabulation of specimen types vs. antibacterials (SPSS output)

**Specimen types Vs. Chloramphenicol (30µg)**

**Crosstab**

| | | | C 30ug | | | |
|---|---|---|---|---|---|---|
| | | | ND | CS | CR | Total |
| Specimen Group | SWAB | Count | 4 | 591 | 143 | 738 |
| | | % within Specimen Group | 0.5% | 80.1% | 19.4% | 100.0% |
| | | % within C30ug | 57.1% | 74.2% | 70.4% | 73.4% |
| | | % of Total | 0.4% | 58.7% | 14.2% | 73.4% |
| | CATHETHER TIP | Count | 0 | 5 | 8 | 13 |
| | | % within Specimen Group | 0.0% | 38.5% | 61.5% | 100.0% |
| | | % within C 30ug | 0.0% | 0.6% | 3.9% | 1.3% |
| | | % of Total | 0.0% | 0.5% | 0.8% | 1.3% |
| | BONE | Count | 0 | 0 | 2 | 2 |
| | | % within Specimen Group | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within C 30ug | 0.0% | 0.0% | 1.0% | 0.2% |
| | | % of Total | 0.0% | 0.0% | 0.2% | 0.2% |
| | ASPIRATE | Count | 0 | 36 | 10 | 46 |
| | | % within Specimen Group | 0.0% | 78.3% | 21.7% | 100.0% |
| | | % within C 30ug | 0.0% | 4.5% | 4.9% | 4.6% |
| | | % of Total | 0.0% | 3.6% | 1.0% | 4.6% |
| | SPUTUM | Count | 2 | 27 | 12 | 41 |
| | | % within Specimen Group | 4.9% | 65.9% | 29.3% | 100.0% |
| | | % within C 30ug | 28.6% | 3.4% | 5.9% | 4.1% |
| | | % of Total | 0.2% | 2.7% | 1.2% | 4.1% |
| | VB | Count | 1 | 115 | 18 | 134 |
| | | % within Specimen Group | 0.7% | 85.8% | 13.4% | 100.0% |
| | | % within C 30ug | 14.3% | 14.4% | 8.9% | 13.3% |
| | | % of Total | 0.1% | 11.4% | 1.8% | 13.3% |
| | URINE | Count | 0 | 19 | 10 | 29 |
| | | % within Specimen Group | 0.0% | 65.5% | 34.5% | 100.0% |
| | | % within C 30ug | 0.0% | 2.4% | 4.9% | 2.9% |
| | | % of Total | 0.0% | 1.9% | 1.0% | 2.9% |
| | CSF | Count | 0 | 2 | 0 | 2 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within C 30ug | 0.0% | 0.3% | 0.0% | 0.2% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % of Total | 0.0% | 0.2% | 0.0% | 0.2% |
| | SCRAPINGS | Count | 0 | 1 | 0 | 1 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within C 30ug | 0.0% | 0.1% | 0.0% | 0.1% |
| | | % of Total | 0.0% | 0.1% | 0.0% | 0.1% |
| Total | | Count | 7 | 796 | 203 | 1006 |
| | | % within Specimen Group | 0.7% | 79.1% | 20.2% | 100.0% |
| | | % within C 30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 0.7% | 79.1% | 20.2% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 43.986[a] | 16 | .001 |
| Likelihood Ratio | 34.246 | 16 | .005 |
| N of Valid Cases | 1006 | | |

a. 15 cells (55.6%) have expected count less than 5. The minimum expected count is .01.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .209 | .001 |
| | Cramer's V | .148 | .000 |
| N of Valid Cases | | 1006 | |

**Specimen types Vs. Erythromycin (15µg)**

**Crosstab**

| | | | E 15 ug | | | |
|---|---|---|---|---|---|---|
| | | | END | ES | ER | Total |
| Specimen Group | SWAB | Count | 45 | 491 | 202 | 738 |
| | | % within Specimen Group | 6.1% | 66.5% | 27.4% | 100.0% |
| | | % within E 15 ug | 84.9% | 72.2% | 74.0% | 73.4% |
| | | % of Total | 4.5% | 48.8% | 20.1% | 73.4% |
| | CATHETHER TIP | Count | 0 | 5 | 8 | 13 |
| | | % within Specimen Group | 0.0% | 38.5% | 61.5% | 100.0% |
| | | % within E 15 ug | 0.0% | 0.7% | 2.9% | 1.3% |
| | | % of Total | 0.0% | 0.5% | 0.8% | 1.3% |
| | BONE | Count | 0 | 2 | 0 | 2 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within E 15 ug | 0.0% | 0.3% | 0.0% | 0.2% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % of Total | 0.0% | 0.2% | 0.0% | 0.2% |
| | ASPIRATE | Count | 2 | 33 | 11 | 46 |
| | | % within Specimen Group | 4.3% | 71.7% | 23.9% | 100.0% |
| | | % within E 15 ug | 3.8% | 4.9% | 4.0% | 4.6% |
| | | % of Total | 0.2% | 3.3% | 1.1% | 4.6% |
| | SPUTUM | Count | 0 | 32 | 9 | 41 |
| | | % within Specimen Group | 0.0% | 78.0% | 22.0% | 100.0% |
| | | % within E 15 ug | 0.0% | 4.7% | 3.3% | 4.1% |
| | | % of Total | 0.0% | 3.2% | 0.9% | 4.1% |
| | VB | Count | 5 | 97 | 32 | 134 |
| | | % within Specimen Group | 3.7% | 72.4% | 23.9% | 100.0% |
| | | % within E 15 ug | 9.4% | 14.3% | 11.7% | 13.3% |
| | | % of Total | 0.5% | 9.6% | 3.2% | 13.3% |
| | URINE | Count | 1 | 17 | 11 | 29 |
| | | % within Specimen Group | 3.4% | 58.6% | 37.9% | 100.0% |
| | | % within E 15 ug | 1.9% | 2.5% | 4.0% | 2.9% |
| | | % of Total | 0.1% | 1.7% | 1.1% | 2.9% |
| | CSF | Count | 0 | 2 | 0 | 2 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within E 15 ug | 0.0% | 0.3% | 0.0% | 0.2% |
| | | % of Total | 0.0% | 0.2% | 0.0% | 0.2% |
| | SCRAPPINGS | Count | 0 | 1 | 0 | 1 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within E 15 ug | 0.0% | 0.1% | 0.0% | 0.1% |
| | | % of Total | 0.0% | 0.1% | 0.0% | 0.1% |
| Total | | Count | 53 | 680 | 273 | 1006 |
| | | % within Specimen Group | 5.3% | 67.6% | 27.1% | 100.0% |
| | | % within E 15 ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 5.3% | 67.6% | 27.1% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 18.434[a] | 16 | .299 |
| Likelihood Ratio | 21.534 | 16 | .159 |
| N of Valid Cases | 1006 | | |

a. 14 cells (51.9%) have expected count less than 5. The minimum expected count is .05.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .135 | .299 |
| | Cramer's V | .096 | .299 |
| N of Valid Cases | | 1006 | |

**Specimen types Vs. Septrin (25µg)**

**Crosstab**

| | | | SXT 25ug | | | |
|---|---|---|---|---|---|---|
| | | | SXTND | SXTS | SXTR | Total |
| Specimen Group | SWAB | Count | 211 | 479 | 48 | 738 |
| | | % within Specimen Group | 28.6% | 64.9% | 6.5% | 100.0% |
| | | % within SXT 25ug | 62.8% | 78.8% | 77.4% | 73.4% |
| | | % of Total | 21.0% | 47.6% | 4.8% | 73.4% |
| | CATHETHER TIP | Count | 5 | 6 | 2 | 13 |
| | | % within Specimen Group | 38.5% | 46.2% | 15.4% | 100.0% |
| | | % within SXT 25ug | 1.5% | 1.0% | 3.2% | 1.3% |
| | | % of Total | 0.5% | 0.6% | 0.2% | 1.3% |
| | BONE | Count | 0 | 2 | 0 | 2 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within SXT 25ug | 0.0% | 0.3% | 0.0% | 0.2% |
| | | % of Total | 0.0% | 0.2% | 0.0% | 0.2% |
| | ASPIRATE | Count | 20 | 23 | 3 | 46 |
| | | % within Specimen Group | 43.5% | 50.0% | 6.5% | 100.0% |
| | | % within SXT 25ug | 6.0% | 3.8% | 4.8% | 4.6% |
| | | % of Total | 2.0% | 2.3% | 0.3% | 4.6% |
| | SPUTUM | Count | 16 | 22 | 3 | 41 |
| | | % within Specimen Group | 39.0% | 53.7% | 7.3% | 100.0% |
| | | % within SXT 25ug | 4.8% | 3.6% | 4.8% | 4.1% |
| | | % of Total | 1.6% | 2.2% | 0.3% | 4.1% |
| | VB | Count | 64 | 68 | 2 | 134 |
| | | % within Specimen Group | 47.8% | 50.7% | 1.5% | 100.0% |
| | | % within SXT 25ug | 19.0% | 11.2% | 3.2% | 13.3% |
| | | % of Total | 6.4% | 6.8% | 0.2% | 13.3% |
| | URINE | Count | 19 | 6 | 4 | 29 |
| | | % within Specimen Group | 65.5% | 20.7% | 13.8% | 100.0% |
| | | % within SXT 25ug | 5.7% | 1.0% | 6.5% | 2.9% |
| | | % of Total | 1.9% | 0.6% | 0.4% | 2.9% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | CSF | Count | 1 | 1 | 0 | 2 |
| | | % within Specimen Group | 50.0% | 50.0% | 0.0% | 100.0% |
| | | % within SXT 25ug | 0.3% | 0.2% | 0.0% | 0.2% |
| | | % of Total | 0.1% | 0.1% | 0.0% | 0.2% |
| | SCRAPPINGS | Count | 0 | 1 | 0 | 1 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 100.0% |
| | | % within SXT 25ug | 0.0% | 0.2% | 0.0% | 0.1% |
| | | % of Total | 0.0% | 0.1% | 0.0% | 0.1% |
| Total | | Count | 336 | 608 | 62 | 1006 |
| | | % within Specimen Group | 33.4% | 60.4% | 6.2% | 100.0% |
| | | % within SXT 25ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 33.4% | 60.4% | 6.2% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 49.710[a] | 16 | .001 |
| Likelihood Ratio | 51.643 | 16 | .000 |
| N of Valid Cases | 1006 | | |

a. 14 cells (51.9%) have expected count less than 5. The minimum expected count is .06.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .222 | .001 |
| | Cramer's V | .157 | .000 |
| N of Valid Cases | | 1006 | |

## Specimen types Vs. Vancomycin (30µg)

**Crosstab**

| | | | VA 30ug | | | | |
|---|---|---|---|---|---|---|---|
| | | | VAND | VAS | VAR | R | Total |
| Specimen Group | SWAB | Count | 3 | 708 | 26 | 1 | 738 |
| | | % within Specimen Group | 0.4% | 95.9% | 3.5% | 0.1% | 100.0% |
| | | % within VA 30ug | 60.0% | 73.7% | 66.7% | 100.0% | 73.4% |
| | | % of Total | 0.3% | 70.4% | 2.6% | 0.1% | 73.4% |
| | CATHETHER TIP | Count | 0 | 12 | 1 | 0 | 13 |
| | | % within Specimen Group | 0.0% | 92.3% | 7.7% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 1.2% | 2.6% | 0.0% | 1.3% |
| | | % of Total | 0.0% | 1.2% | 0.1% | 0.0% | 1.3% |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | BONE | Count | 0 | 2 | 0 | 0 | 2 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 0.2% | 0.0% | 0.0% | 0.2% |
| | | % of Total | 0.0% | 0.2% | 0.0% | 0.0% | 0.2% |
| | ASPIRATE | Count | 0 | 44 | 2 | 0 | 46 |
| | | % within Specimen Group | 0.0% | 95.7% | 4.3% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 4.6% | 5.1% | 0.0% | 4.6% |
| | | % of Total | 0.0% | 4.4% | 0.2% | 0.0% | 4.6% |
| | SPUTUM | Count | 1 | 35 | 5 | 0 | 41 |
| | | % within Specimen Group | 2.4% | 85.4% | 12.2% | 0.0% | 100.0% |
| | | % within VA 30ug | 20.0% | 3.6% | 12.8% | 0.0% | 4.1% |
| | | % of Total | 0.1% | 3.5% | 0.5% | 0.0% | 4.1% |
| | VB | Count | 1 | 129 | 4 | 0 | 134 |
| | | % within Specimen Group | 0.7% | 96.3% | 3.0% | 0.0% | 100.0% |
| | | % within VA 30ug | 20.0% | 13.4% | 10.3% | 0.0% | 13.3% |
| | | % of Total | 0.1% | 12.8% | 0.4% | 0.0% | 13.3% |
| | URINE | Count | 0 | 28 | 1 | 0 | 29 |
| | | % within Specimen Group | 0.0% | 96.6% | 3.4% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 2.9% | 2.6% | 0.0% | 2.9% |
| | | % of Total | 0.0% | 2.8% | 0.1% | 0.0% | 2.9% |
| | CSF | Count | 0 | 2 | 0 | 0 | 2 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 0.2% | 0.0% | 0.0% | 0.2% |
| | | % of Total | 0.0% | 0.2% | 0.0% | 0.0% | 0.2% |
| | SCRAPPINGS | Count | 0 | 1 | 0 | 0 | 1 |
| | | % within Specimen Group | 0.0% | 100.0% | 0.0% | 0.0% | 100.0% |
| | | % within VA 30ug | 0.0% | 0.1% | 0.0% | 0.0% | 0.1% |
| | | % of Total | 0.0% | 0.1% | 0.0% | 0.0% | 0.1% |
| Total | | Count | 5 | 961 | 39 | 1 | 1006 |
| | | % within Specimen Group | 0.5% | 95.5% | 3.9% | 0.1% | 100.0% |
| | | % within VA 30ug | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 0.5% | 95.5% | 3.9% | 0.1% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 13.270[a] | 24 | .961 |
| Likelihood Ratio | 9.905 | 24 | .995 |
| N of Valid Cases | 1006 | | |

a. 28 cells (77.8%) have expected count less than 5. The minimum expected count is .00.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .115 | .961 |
| | Cramer's V | .066 | .961 |
| N of Valid Cases | | 1006 | |

## Specimen types Vs. Tetracycline (30µg)

**Crosstab**

| | | | TE 30ug | | | |
|---|---|---|---|---|---|---|
| | | | TEND | TER | TES | Total |
| Specimen Group | SWAB | Count | 8 | 41 | 689 | 738 |
| | | % within Specimen Group | 1.1% | 5.6% | 93.4% | 100.0% |
| | | % within TE 30ug | 66.7% | 67.2% | 73.8% | 73.4% |
| | | % of Total | 0.8% | 4.1% | 68.5% | 73.4% |
| | CATHETHER TIP | Count | 0 | 2 | 11 | 13 |
| | | % within Specimen Group | 0.0% | 15.4% | 84.6% | 100.0% |
| | | % within TE 30ug | 0.0% | 3.3% | 1.2% | 1.3% |
| | | % of Total | 0.0% | 0.2% | 1.1% | 1.3% |
| | BONE | Count | 0 | 0 | 2 | 2 |
| | | % within Specimen Group | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within TE 30ug | 0.0% | 0.0% | 0.2% | 0.2% |
| | | % of Total | 0.0% | 0.0% | 0.2% | 0.2% |
| | ASPIRATE | Count | 0 | 2 | 44 | 46 |
| | | % within Specimen Group | 0.0% | 4.3% | 95.7% | 100.0% |
| | | % within TE 30ug | 0.0% | 3.3% | 4.7% | 4.6% |
| | | % of Total | 0.0% | 0.2% | 4.4% | 4.6% |
| | SPUTUM | Count | 0 | 2 | 39 | 41 |
| | | % within Specimen Group | 0.0% | 4.9% | 95.1% | 100.0% |
| | | % within TE 30ug | 0.0% | 3.3% | 4.2% | 4.1% |
| | | % of Total | 0.0% | 0.2% | 3.9% | 4.1% |
| | VB | Count | 4 | 7 | 123 | 134 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | % within Specimen Group | 3.0% | 5.2% | 91.8% | 100.0% |
| | | % within TE 30ug | 33.3% | 11.5% | 13.2% | 13.3% |
| | | % of Total | 0.4% | 0.7% | 12.2% | 13.3% |
| | URINE | Count | 0 | 7 | 22 | 29 |
| | | % within Specimen Group | 0.0% | 24.1% | 75.9% | 100.0% |
| | | % within TE 30ug | 0.0% | 11.5% | 2.4% | 2.9% |
| | | % of Total | 0.0% | 0.7% | 2.2% | 2.9% |
| | CSF | Count | 0 | 0 | 2 | 2 |
| | | % within Specimen Group | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within TE 30ug | 0.0% | 0.0% | 0.2% | 0.2% |
| | | % of Total | 0.0% | 0.0% | 0.2% | 0.2% |
| | SCRAPPINGS | Count | 0 | 0 | 1 | 1 |
| | | % within Specimen Group | 0.0% | 0.0% | 100.0% | 100.0% |
| | | % within TE 30ug | 0.0% | 0.0% | 0.1% | 0.1% |
| | | % of Total | 0.0% | 0.0% | 0.1% | 0.1% |
| Total | | Count | 12 | 61 | 933 | 1006 |
| | | % within Specimen Group | 1.2% | 6.1% | 92.7% | 100.0% |
| | | % within TE 30ug | 100.0% | 100.0% | 100.0% | 100.0% |
| | | % of Total | 1.2% | 6.1% | 92.7% | 100.0% |

**Chi-Square Tests**

| | Value | Df | Asymptotic Significance (2-sided) |
|---|---|---|---|
| Pearson Chi-Square | 24.981[a] | 16 | .070 |
| Likelihood Ratio | 18.593 | 16 | .290 |
| N of Valid Cases | 1006 | | |

a. 18 cells (66.7%) have expected count less than 5. The minimum expected count is .01.

**Symmetric Measures**

| | | Value | Approximate Significance |
|---|---|---|---|
| Nominal by Nominal | Phi | .158 | .070 |
| | Cramer's V | .111 | .070 |
| N of Valid Cases | | 1006 | |