



DRUG USE EVALUATION REPORT

**Investigating Meropenem usage at the Colonial War
Memorial Hospital from October 2013 to October 2014**

MARCH 2015



Acknowledgements

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DRUG USE EVALUATION

Meropenem usage at the Colonial War Memorial Hospital

Introduction

Meropenem is a broad-spectrum antibacterial agent, with activity against the majority of Gram positive, Gram negative and anaerobic bacteria. As such, its use and misuse raises the potential for the development of significant bacterial resistance with profound clinical impact on the Fijian healthcare system. In addition, meropenem is very expensive with the current procurement cost of meropenem at \$8.82 for a 500 mg vial. For these two reasons, meropenem use at the three Divisional Hospitals including the Colonial War Memorial Hospital (CWMH) must be strictly limited. Recently, bacterial resistance to meropenem has emerged in the Divisional Hospitals and use of the last line antibiotic colistin has become necessary.

According to the *Indications for Meropenem Use at Divisional Hospitals Policy*, (Appendix 1), meropenem is indicated for;

1. *Any individual patient where there is a clear clinical evidence of infection*

PLUS

A blood culture plus other relevant body fluids confirmed positive for an organism shown to be resistant to all other available (or appropriate) antibiotics.

2. *A confirmed outbreak of an organism resistant to all other available (or appropriate) antibiotics in the Intensive Care Units only (NICU, PICU or adult ICU), as **empirical therapy for patients with clinical evidence of infection, for a maximum of 72 hours pending results of microbiology specimens. If infection with a multi-resistant organism is not microbiologically confirmed at this time, meropenem must be ceased and appropriate alternative antimicrobial therapy instituted.** Once the outbreak is declared controlled by the Infection Control Unit, empirical antibiotic therapy must revert to a non-Meropenem containing regimen.*

In both situations the duration of treatment should be the decision of the treatment Consultant.

This study was undertaken to investigate the reasons for the increased meropenem consumption in the Divisional hospitals of Fiji which has risen nearly forty-fold since 2007 (Appendix 2). The study will provide recommendations for interventions to increase rational use of meropenem and decrease the consumption and prevent further antimicrobial resistance in CWMH. Further studies to investigate use at the Labasa and Lautoka Divisional hospitals are highly recommended.

Summary

A drug use evaluation was performed investigating the usage of meropenem at the Colonial War Memorial Hospital between October 2013 and October 2014. Data from the *Restricted Antimicrobial Request Form*, pharmacy dispensing program PatisPlus® and microbiology laboratory records were used to analyse the prescribing of meropenem compared to the *Indications for Meropenem use at Divisional Hospitals Policy* and treatment guidelines. Infection control unit nurses, Pharmacy department staff and the head of the Microbiology department were interviewed, prescribers were surveyed and an infectious disease prescriber was consulted to provide prescriber related comments. It was found that meropenem use can be optimised in several areas including; appropriate dosing, use of sensitivity data, infection control and prevention and stock management. A few of the critical interventions recommended to address these problems include; the updating of the *Indications for Meropenem use at Divisional Hospitals Policy*, development of the *Meropenem Treatment Guideline*, microbiology results be made available on PatisPlus®, development of stock management standard operating procedures and all cases of multi-resistant organisms to be treated as an outbreak.

Aim

To assess the usage of meropenem at the Colonial War Memorial Hospital compared to the *Indications for Meropenem use at Divisional Hospitals Policy* and standard treatment guidelines and provide recommendations to improve rational use of meropenem at CWMH and reduce the development of further antibiotic resistance.

Method

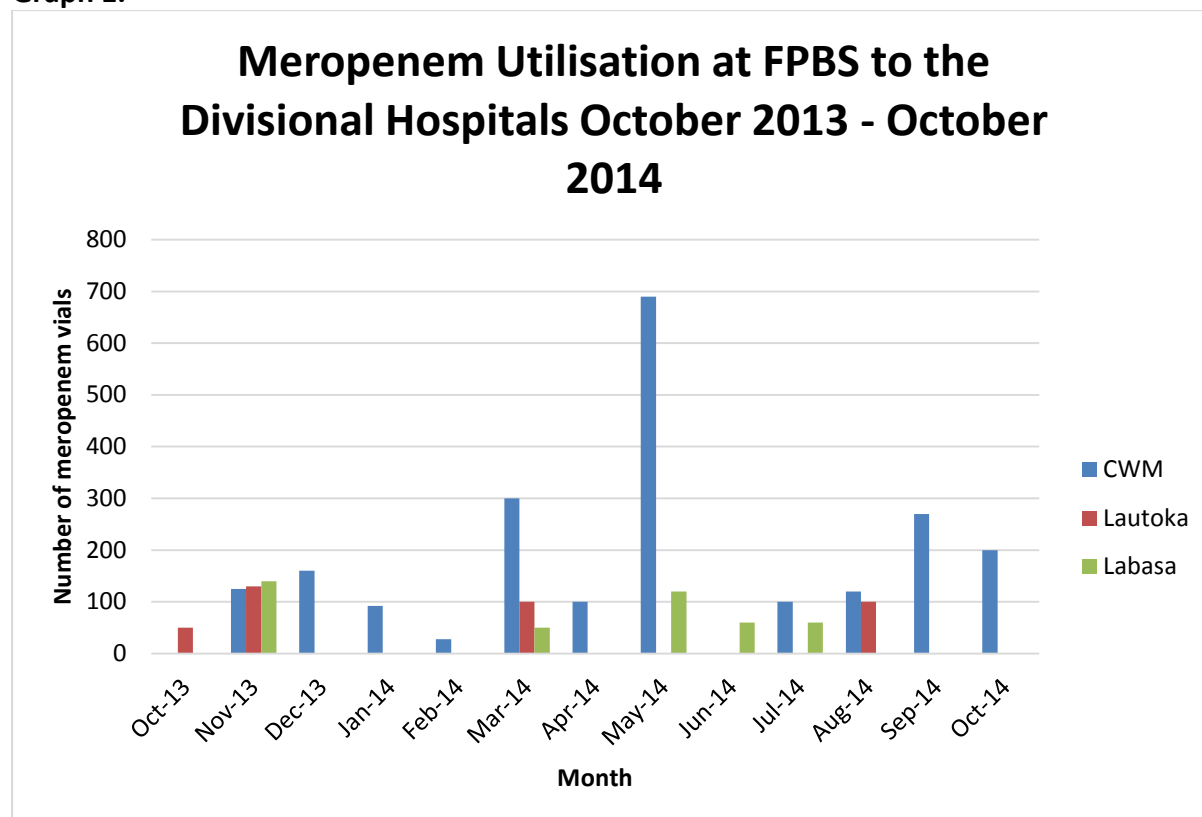
A retrospective observational cohort study of meropenem usage at CWMH was conducted using data from the *Restricted Antimicrobial Request Form* (Appendix 3), microbiology laboratory records and inpatient pharmacy dispensing records on PatisPlus®. The data was collated and entered into the Excel® data collection spread sheet (Appendix 4) for every patient prescribed meropenem between 1 October 2013 and 31 October 2014. The data collection was conducted over a two week period between 24 November 2014 and 6 December 2014. A survey (Appendix 5) was also distributed to CWMH prescribers during this time.

A tour of CWMH's three intensive care units (ICUs) was undertaken on 6 December 2014 to establish the context of the results and observe relevant infrastructure and facilities such as the hand hygiene stations, infection control posters and protocols and isolation units. On 12 February 2015, the head of the Microbiology department and the Infection Control unit nurses were interviewed to further analyse potential areas for recommended interventions. An infectious disease prescriber from CWMH provided prescriber related comments via email and the FPBS and Pharmacy department staff were interviewed and emailed for comments regarding stock management and dosage data.

Results

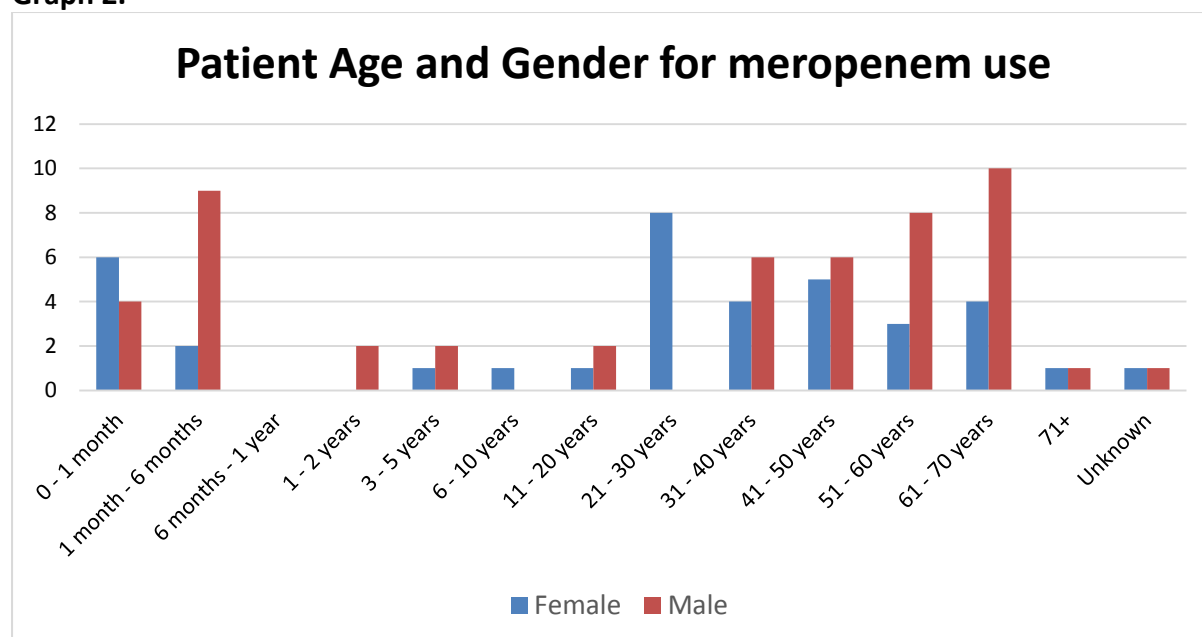
MEROPENEM USAGE

Graph 1.



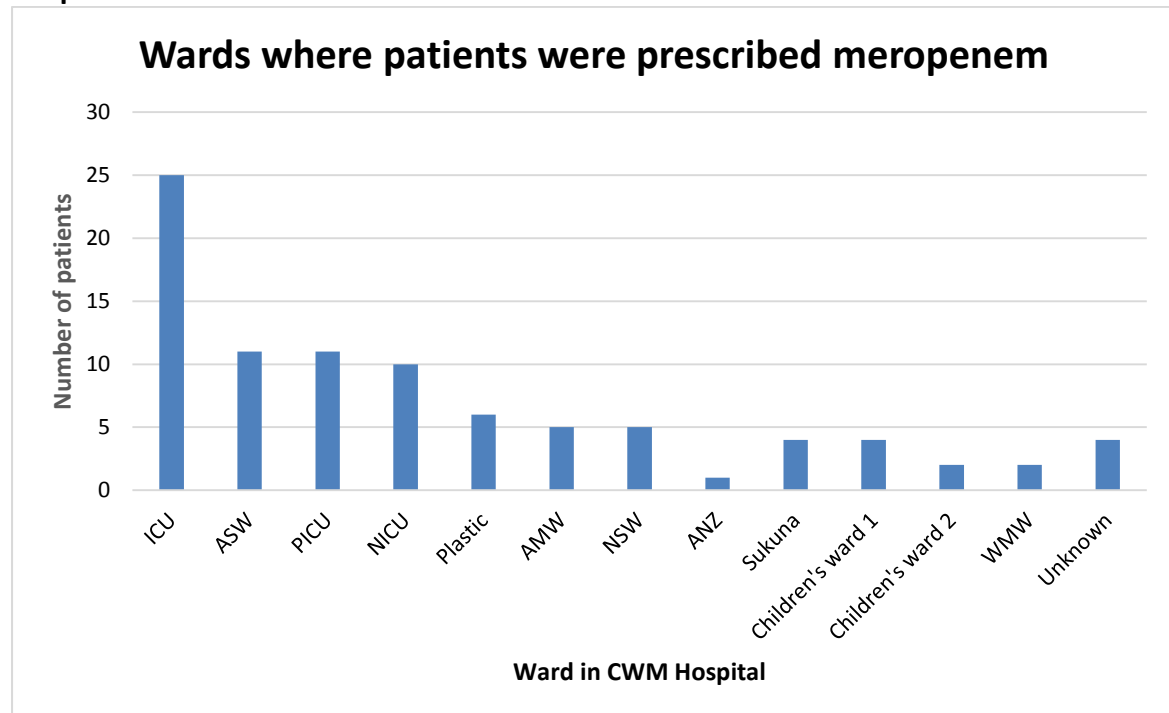
Graph 1 shows meropenem utilisation at FPBS to all of the three Divisional hospitals from October 2013 to October 2014. CWMH was distributed 2185 (74%), Lautoka 330 (11%) and Labasa 430 (15%) of the 2945 vials issued by FPBS during the study period.

Graph 2.



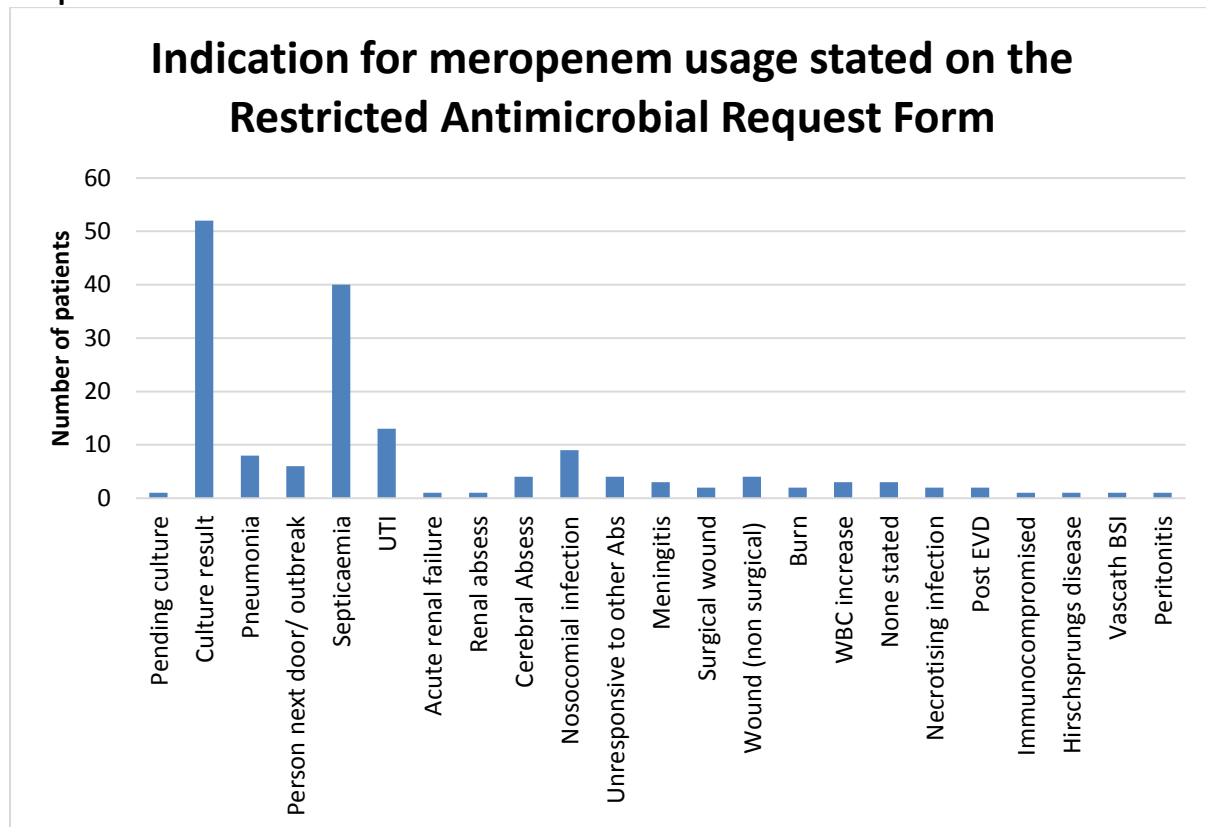
Data from a total of 88 patients were recorded in this study, including 37 females and 51 males. Twenty-four percent of patients studied were less than one year old, with 47.5% of these less than 1 month old. The oldest male was 86 years of age and the oldest female 74 years of age. The age and gender distribution of the patients is shown in Graph 2. Two patients could not be found on PatisPlus® and did not have their age recorded on the *Restricted Antimicrobial Request Form* therefore, their age remains unknown.

Graph 3.



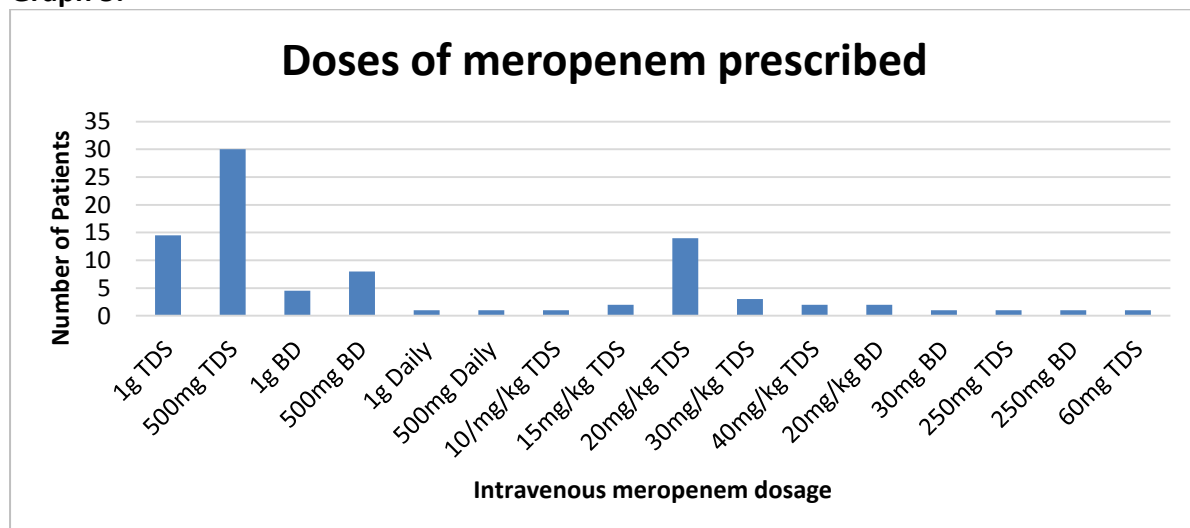
Between October 2013 and October 2014, eleven of the 22 wards at CWMH treated patients with meropenem. Adult ICU housed 28.7% of all patients that used meropenem and the patient's ward was not recorded on 4.6% of patient *Restricted Antimicrobial Request Forms*, therefore, this data is marked as unknown in Graph 3. Meropenem use in children's wards (NICU, PICU, CHWRD1 and CHWRD2) equates to 32.2% of the total number of patients treated with meropenem.

Graph 4.



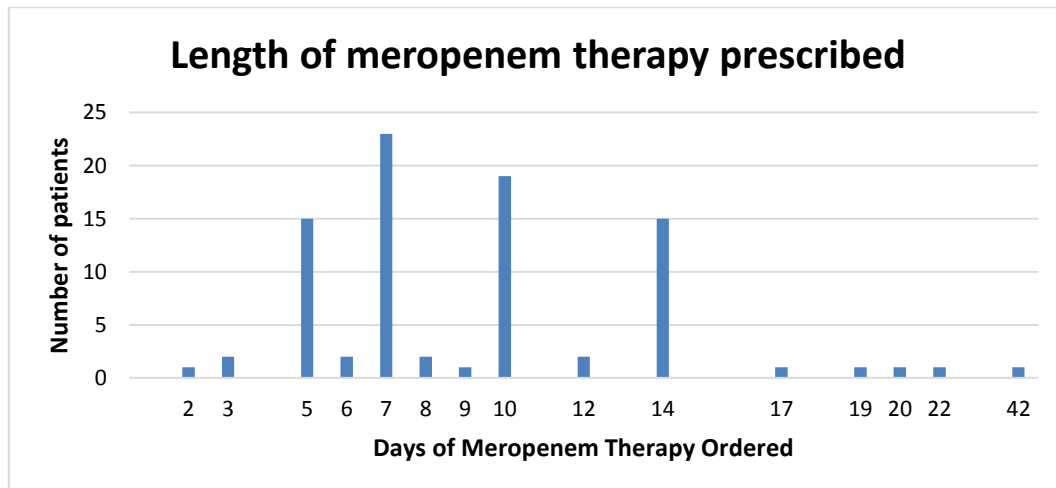
The most common indication stated on the *Restricted Antimicrobial Request Form*, was ‘culture result’ with 59% of all patients treated with meropenem. Septicaemia was the second most common indication with 45% of patients, followed by urinary tract infection (UTI) which accounted for 15% of patients. If more than one indication was recorded on the *Restricted Antimicrobial Request Form*, each is recorded separately in Graph 4.

Graph 5.



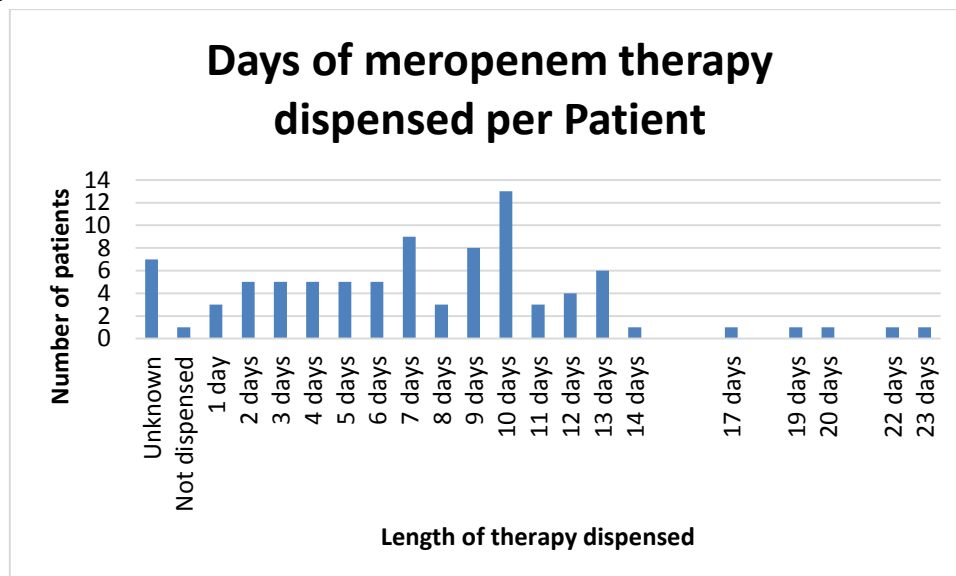
Each patient’s dosing regimen as recorded on the *Restricted Antimicrobial Request Form* for meropenem is shown on Graph 5. Thirty-four percent of patients were prescribed 500 mg three times per day (TDS), with 2.5% prescribed a once daily dose and 19% of patients prescribed twice daily (BD) regimens.

Graph 6.



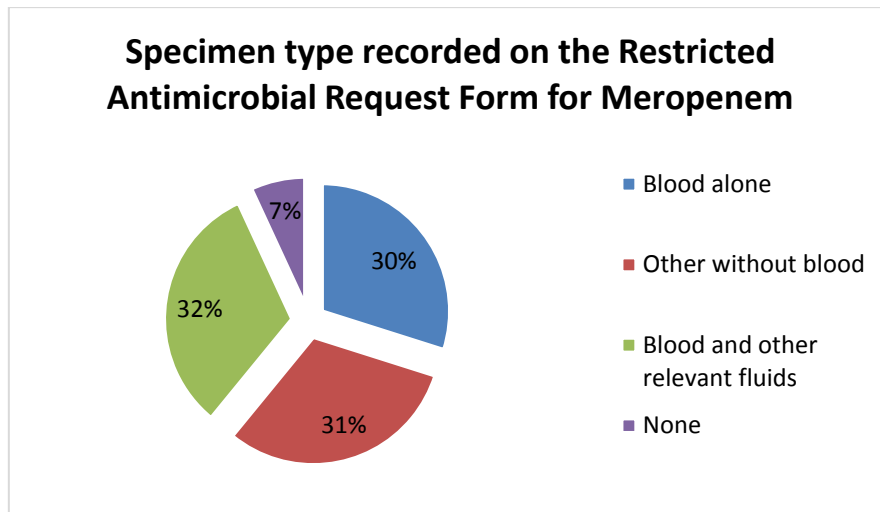
Graph 6 shows the length of therapy prescribed according to the *Restricted Antimicrobial Request Forms*. The average length of therapy prescribed was 9.5 days.

Graph 7.



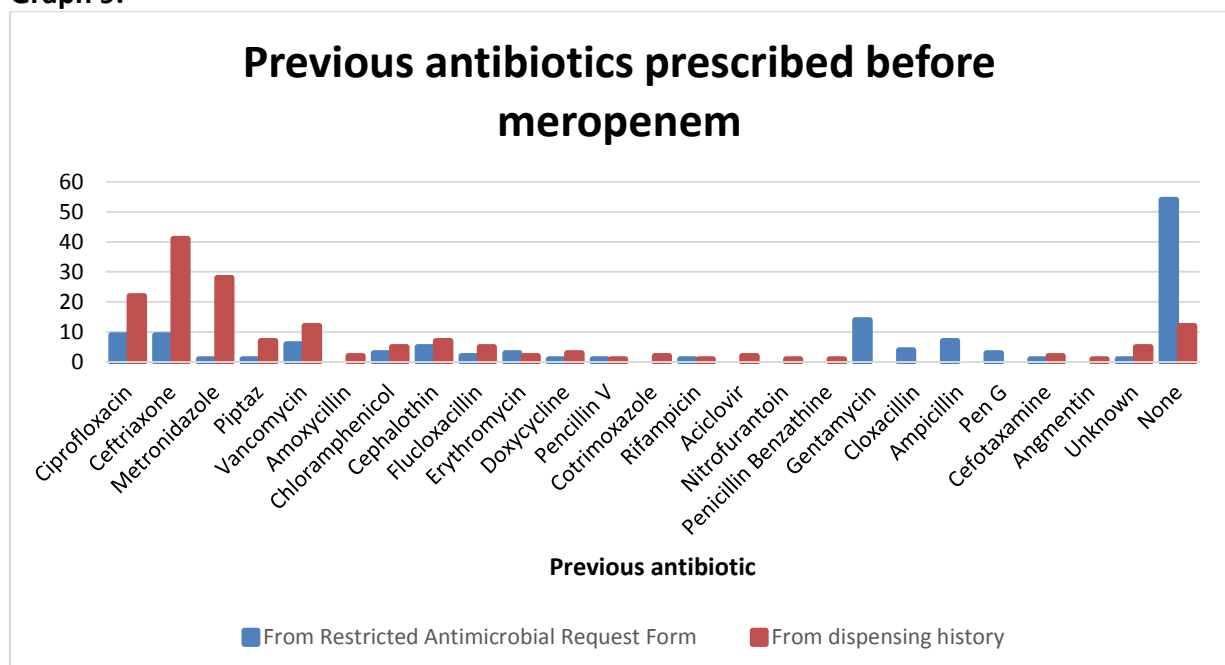
Dispensing data was also used to ascertain the average length of therapy and this dispensing data is shown in Graph 7. The average length of therapy according to the dispensing data is seven and a half days, two days shorter than originally prescribed. The longest meropenem therapy prescribed and dispensed was 42 days. The shortest was a singular dose which was prescribed as a STAT dose during an indwelling catheter change and then commenced two days later.

Graph 8.



It is required in the *Indication for Meropenem Use at Divisional Hospitals Policy*, that organisms be confirmed by cultures of blood and other relevant body fluids. The specimens taken for culture in patients using meropenem in the period of October 2013 to October 2014 is summarised in Graph 8. It was found that 37.9% of patients had no blood culture taken, 18% of which had no specimen taken at all according to their *Restricted Antimicrobial Request Form*. At least one blood culture and one other microbiological test was taken for 32.2% of the patients prescribed meropenem. The remaining 29.9% only had blood cultures taken. These results are only for specimens recorded on the *Restricted Antimicrobial Request Form* and this is unlikely to be the only culture taken for these patients. It was not practical to search the laboratory data books for all specimen results for these patients.

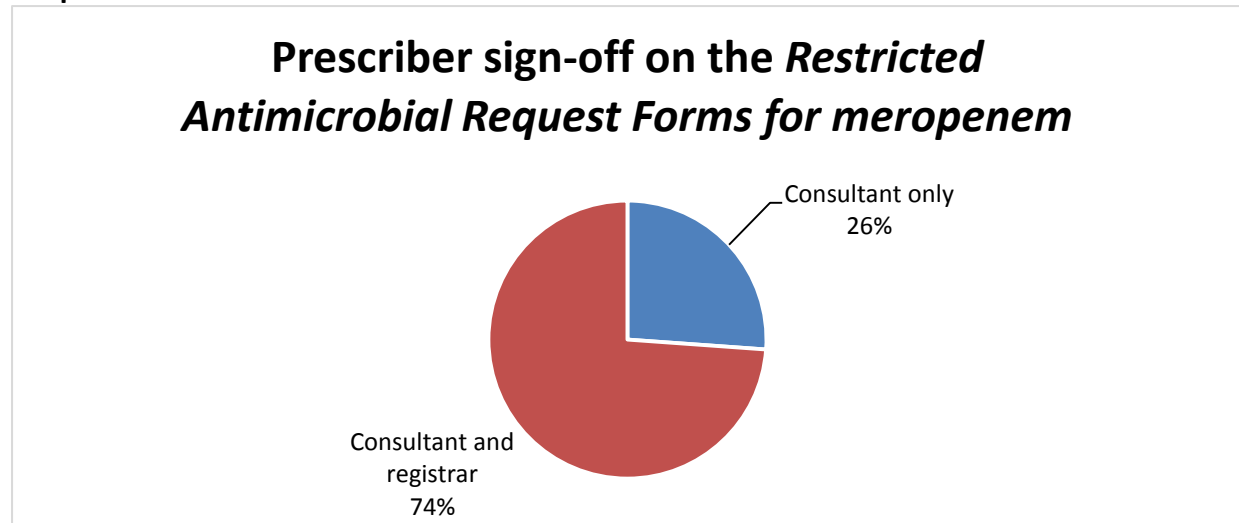
Graph 9.



Graph 9 shows the difference between other antibiotics tried according to the *Restricted Antimicrobial Request Form* and the dispensing history. The dispensing histories do not include medication kept on the wards imprest. The medication kept on imprest varies according to the ward.

The majority of wards included in this study have gentamicin, cloxacillin, ampicillin and benzyl penicillin on imprest hence these were recorded to a greater extent on the *Restricted Antimicrobial Request Form*, compared to the pharmacy dispensary system as imprest items are not dispensed. Graph 9 shows that the form has not been submitted completely as 20% of cases where ceftriaxone had been previously tried, were not recorded by the prescriber.

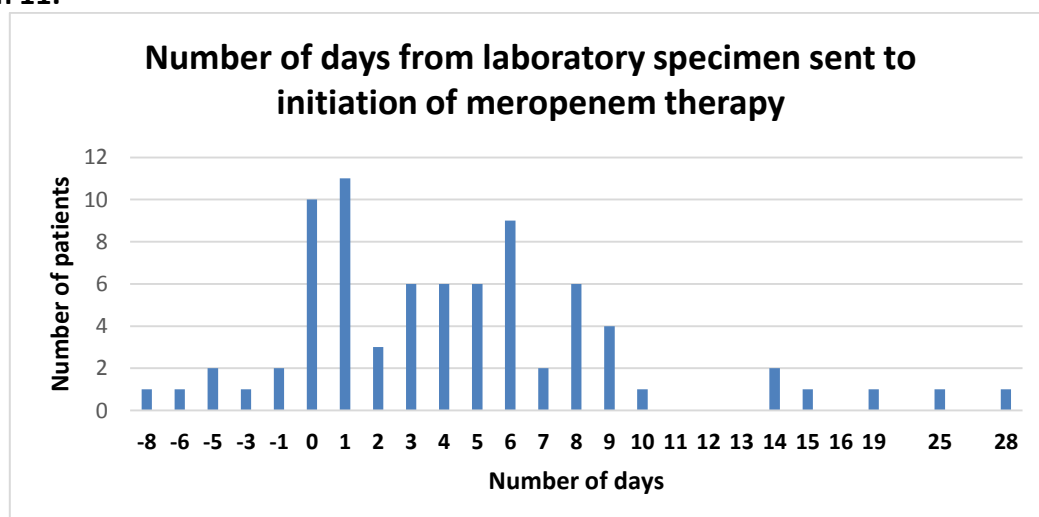
Graph 10.



As part of the *Indications for Meropenem Use at Divisional Hospitals Policy*, a consultant must oversee and sign off on the use of meropenem. On the *Restricted Antimicrobial Request form* there is a space for both a registrar and consultant to sign. Graph 10 shows that a consultant signed every form in the study period as required.

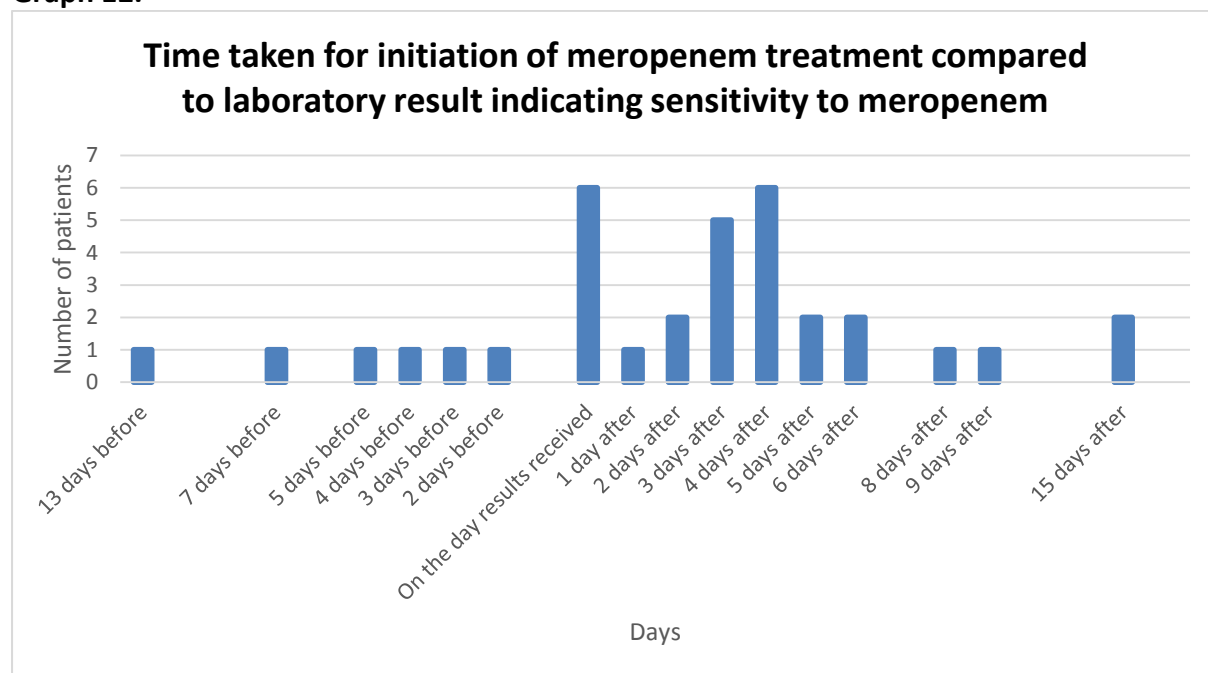
On the *Restricted Antimicrobial Request Form*, there is a section for 'justification for therapy by prescriber.' For 52.3% of patients, no justification was recorded. Where justifications were stated, all were found to be valid. Justifications included organisms found to be resistant to all other available (or appropriate) antibiotics. In 7% of cases, other sensitive antibiotics being out of stock was part of the justification. Culture results indicating meropenem sensitivity was the prescriber's justification in 40% of cases. Having tried other antibiotics with no improvement was cited as justification in 26% of cases. Outbreak and ventilator contaminations were also stated as justifications for therapy.

Graph 11.



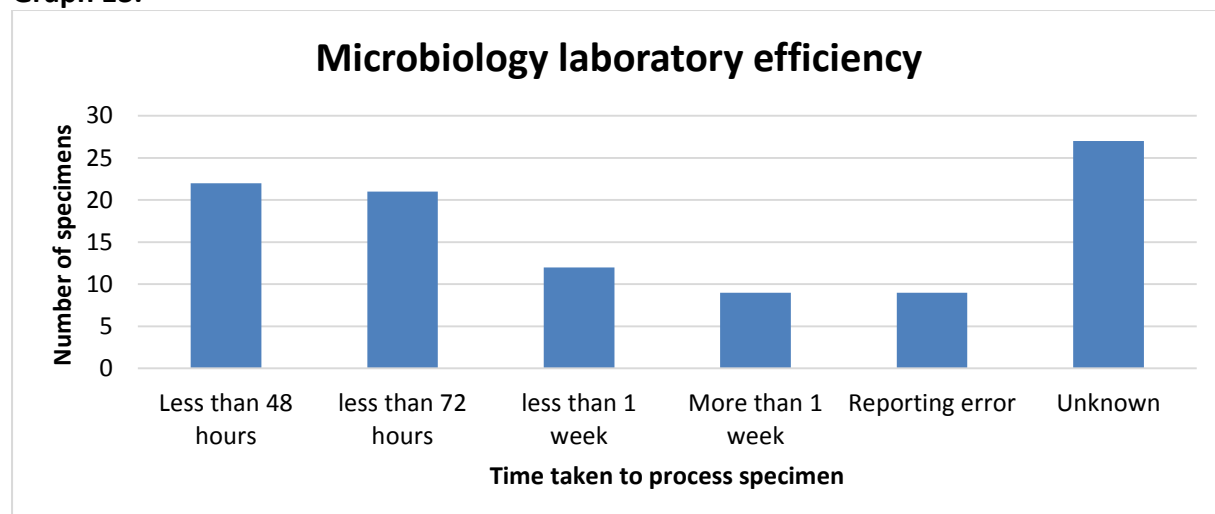
The number of days between the *Restricted Antimicrobial Request Forms* being completed and meropenem therapy being initiated is shown on Graph 11. On average it took 4 days from the form being sent to meropenem therapy being initiated. Compared to the form being sent, the earliest meropenem therapy was initiated was 8 days beforehand. The date the *Restricted Antimicrobial Request Form* was completed is taken from the 'Date specimen taken & sent to lab' section of the form as the date below the consultant's signature was rarely written.

Graph 12.



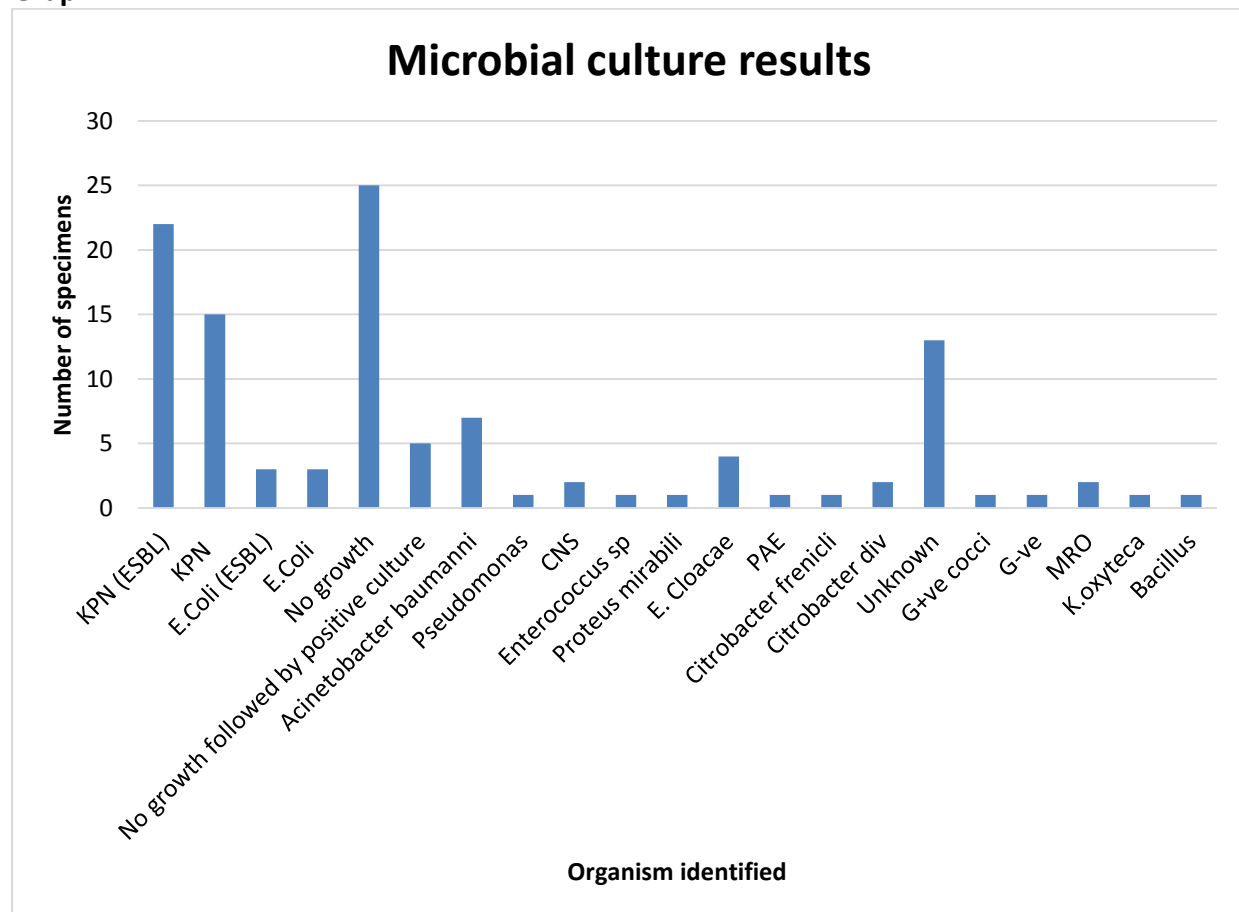
Once laboratory results indicating sensitivity to meropenem became available, Graph 12 shows that the majority of patients were not immediately initiated on meropenem. If the first choice of therapy was not meropenem, the time between therapy with other drugs and the laboratory results is recorded. The average time from results becoming available to initiation of meropenem therapy was two and a half days.

Graph 13.



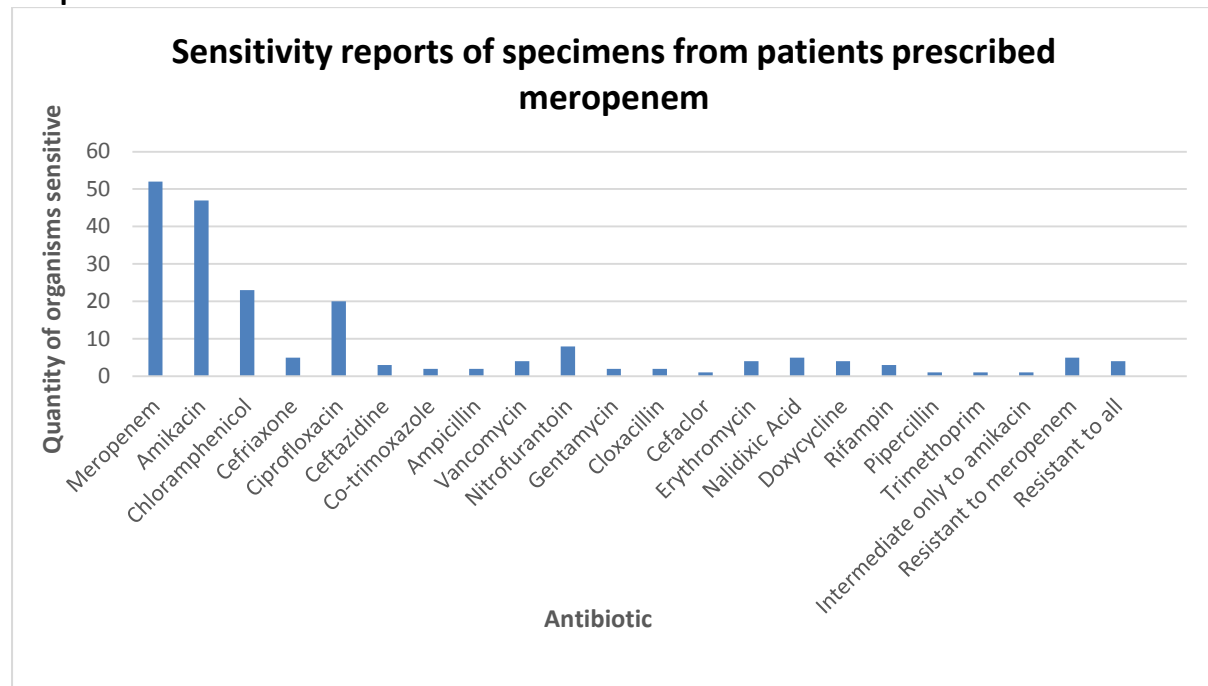
Graph 13 shows the length of time taken to process each specimen for the meropenem patients. 'Reporting error' refers to results that were reported as being available before the specimen was sent, this is logistically impossible, therefore there is an error in reporting of laboratory results or the information given on the *Restricted Antimicrobial Request Form*. The laboratory efficiency of 27% of the specimens is unknown because the date of either the results or the specimen being taken was not recorded. Twenty-five percent of results took less than 48 hours and 24% of results were available within 48 to 72 hours.

Graph 14.



The laboratory results for each culture are recorded in Graph 14. For the specimens ordered on the *Restricted Antimicrobial Request form*, 9.5% have unknown results because the result was not recorded on the form and could not be found in the laboratory records. The most common organism found was *Klebsiella pneumonia* (KPN) with *extended spectrum beta-lactamase* (ESBL). KPN (ESBL) made up 32% of all positive results.

Graph 15

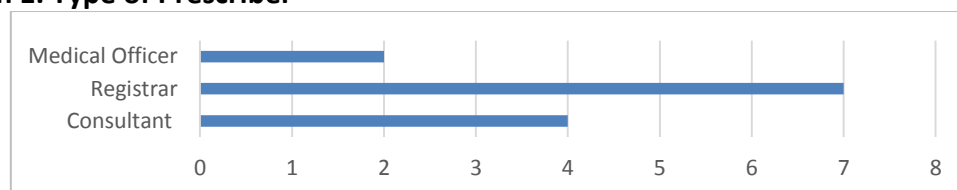


Fifty-five of the 88 patients (62.5%) had sensitivity data recorded. Graph 15 shows the sensitivities for all the specimens taken from patients treated with meropenem. A total of 72 organisms from 55 patients had sensitivities recorded, 62 (86%) of these were sensitive to meropenem; some patients had more than one specimen and more than one organism was isolated. Four organisms were resistant to all available antibiotics, another resistant to all available antibiotics and intermediate to amikacin and a further five were resistant to meropenem. Seventy-two percent of organisms were sensitive to meropenem, 44% of which were also sensitive to chloramphenicol and 38.5% sensitive to ciprofloxacin. Antibiotics being out of stock were cited as the reason for not using another antibiotic in 6 cases (7%). In at least two cases an antibiotic reported as sensitive was tried with no patient improvement.

PRESCRIBER SURVEY

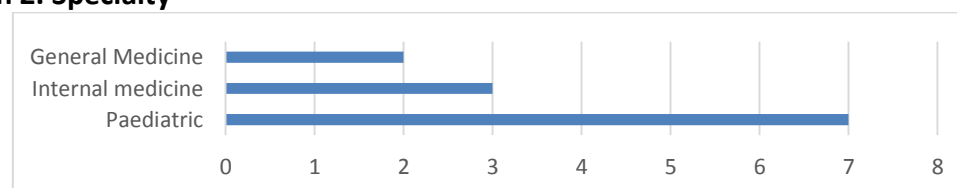
Thirteen prescribers responded to the 13 question survey and gave the following answers.

Question 1. Type of Prescriber



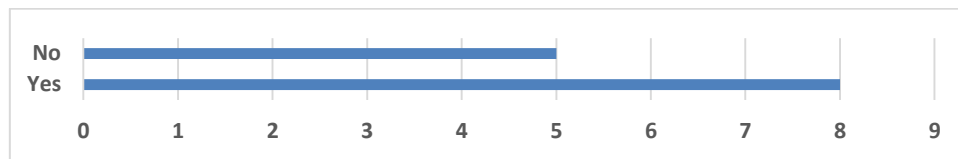
Of the 13 prescribers surveyed, 7 were registrars, 4 consultants and 2 medical officers.

Question 2. Specialty



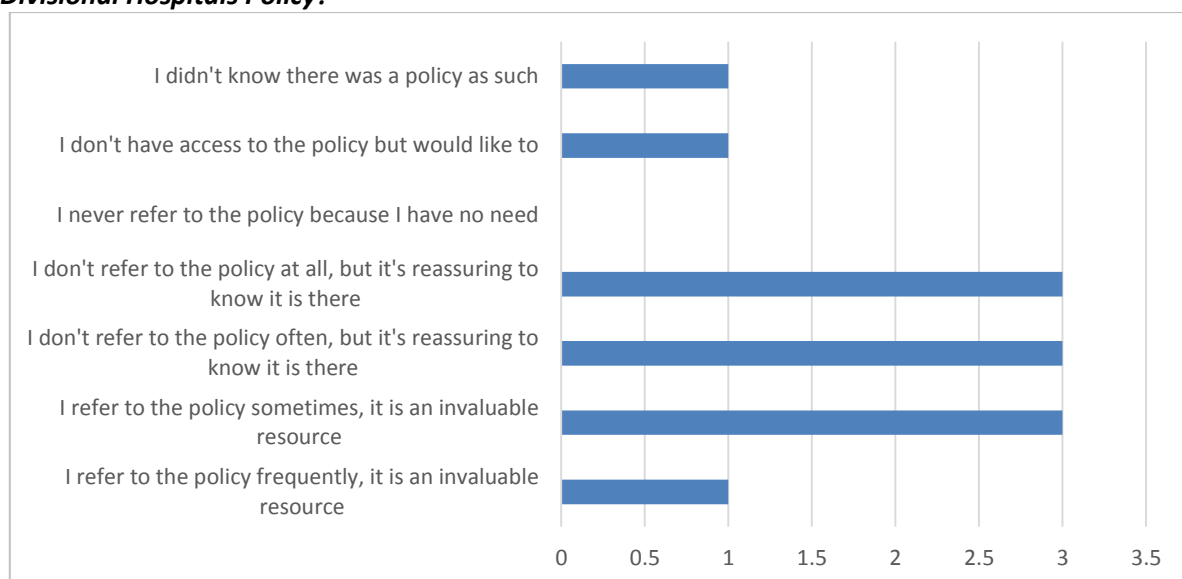
Specialities of the prescribers included 2 from general medicine, 3 internal medicine specialists and 7 paediatric specialists.

Question 3. Are you aware of the *Indications for Meropenem Use at Divisional Hospitals Policy*?



Five out of 13 prescribers were unaware of the *Indications for Meropenem Use at Divisional Hospitals Policy*.

Question 4. Which one of the following best describes your feelings about and use of the *Divisional Hospitals Policy*?



One prescriber was unaware of the Policy, one didn't have access to the policy but would like to. Three prescribers didn't refer to the policy at all, another 3 refer to the policy often and 3 prescribers referred to the policy sometimes and thought it is an invaluable resource. One prescriber referred to the policy frequently and thought it was also an invaluable resource.

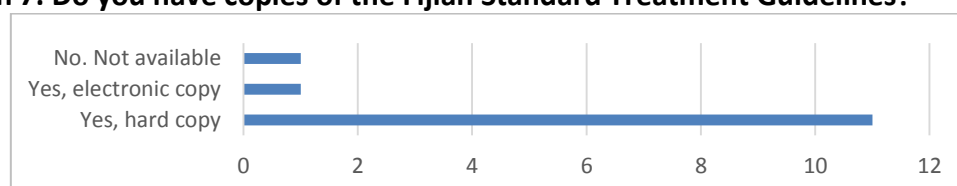
Question 5. Are you aware of the *Restricted Antimicrobial Request Form*?

100% of the surveyed prescribers answered yes.

Question 6. Do you use it every time you prescribe meropenem?

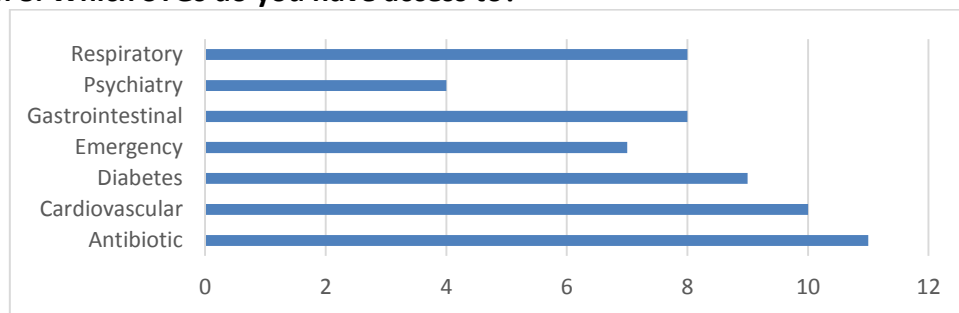
100% of the surveyed prescribers answered yes.

Question 7. Do you have copies of the Fijian Standard Treatment Guidelines?



Twelve prescribers have access to the Fijian Standard Treatment Guidelines (STGs) and one did not have access to the Guidelines at all.

Question 8. Which STGs do you have access to?



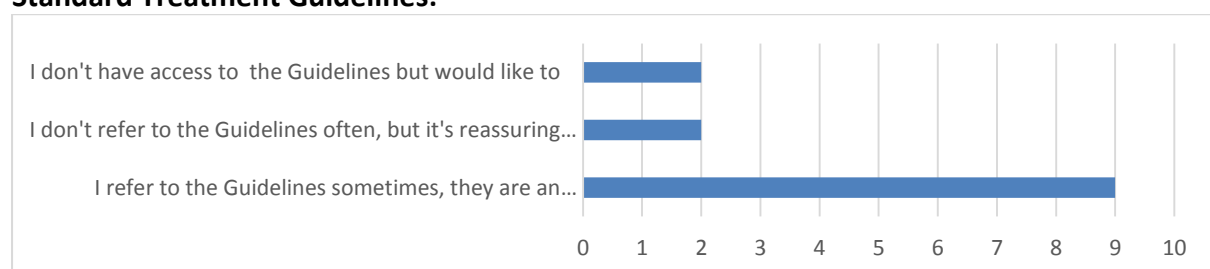
Eleven prescribers had access to the Antibiotic Guidelines, followed by 10 prescribers accessing the Cardiovascular, 9 Diabetes, 8 Gastrointestinal and Respiratory, 7 Emergency and 4 having access to Psychiatry.

Question 9. During your practise do you refer to them:



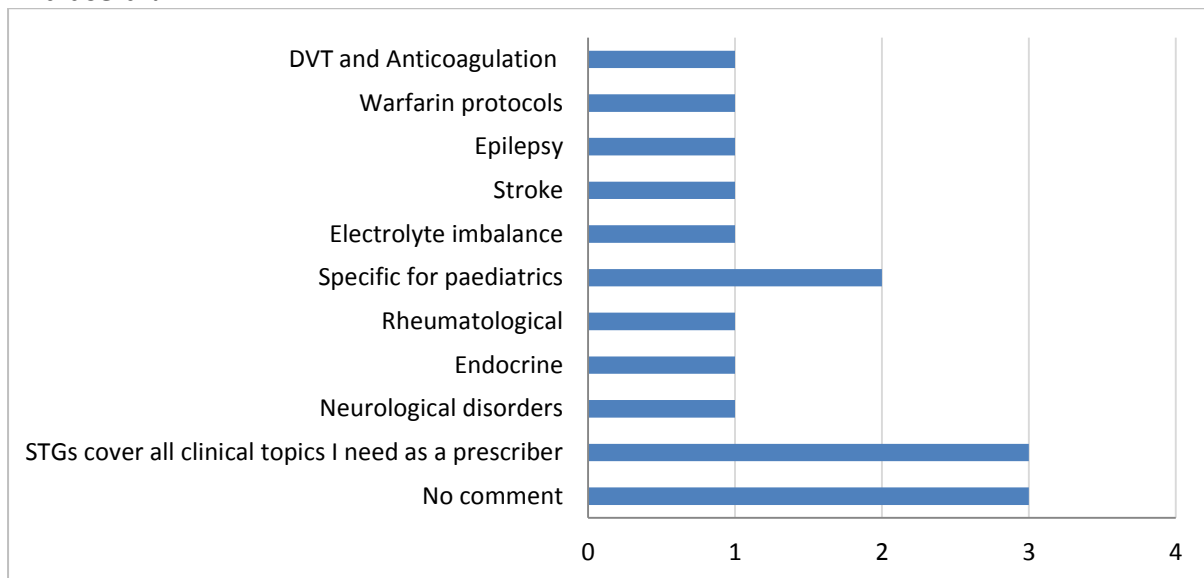
Five prescribers refer to the Guidelines monthly, 4 less than monthly and one prescriber each: didn't have the guidelines, rarely use the guidelines, very familiar with the guidelines and doesn't need to refer to them and used the guidelines weekly.

Question 10. Which one of the following best describes your feelings about and use of Standard Treatment Guidelines:



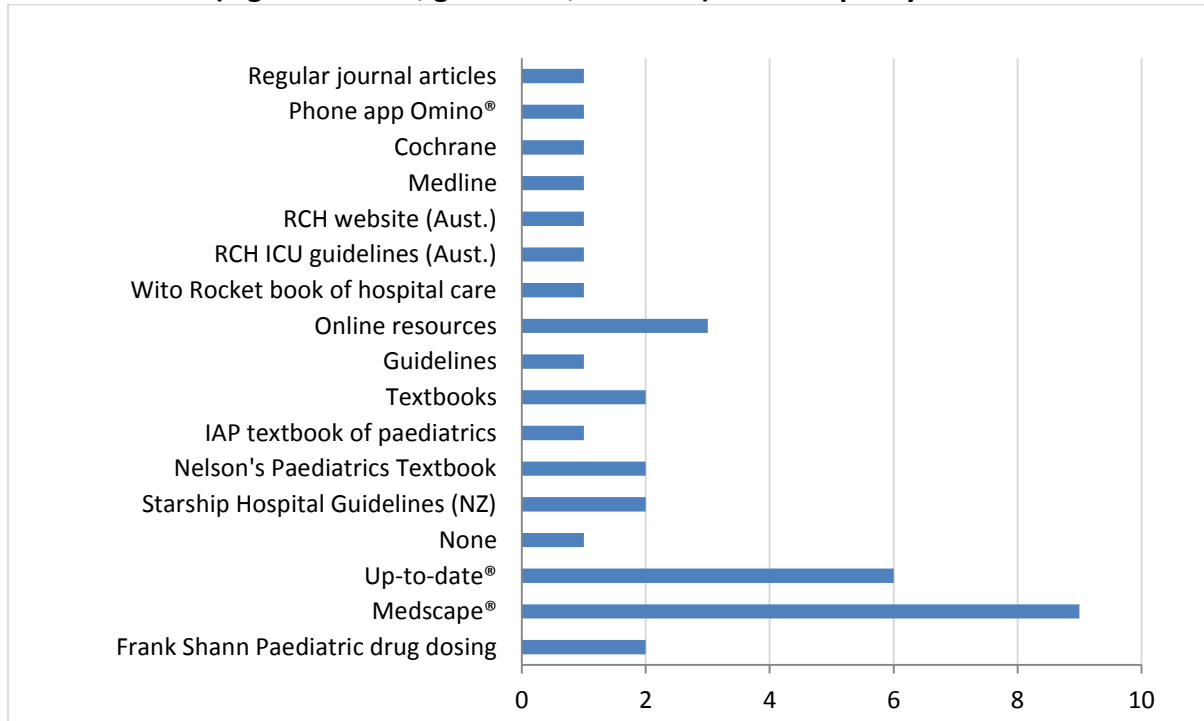
Nine prescribers refer to the Guidelines sometimes and they are an invaluable resource, two don't refer to them often but find it reassuring to know they are there and two prescribers don't have access to the Guidelines but would like to.

Question 11. Are there any clinical topics not currently covered in the STGs that you would find useful?



Three prescribers did not comment and another three stated that STGs cover all clinical topics needed as a prescriber. Two prescribers wanted clinical topics specific for paediatrics and the following suggestions were stated: DVT and anticoagulation, warfarin protocols, epilepsy, stroke, electrolyte imbalance, rheumatological, endocrine and neurological disorders.

Question 12. What other resources do you refer to for information on the management of STG conditions (e.g. text books, guidelines, websites)? Please specify.



Nine prescribers stated Medscape®, 6 Up-to-date®, 3 online resources, 2 each for: Frank Shann Paediatric drug dosing, Starship Hospital Guidelines, Nelson's Paediatrics Textbook and general textbooks. Prescribers also stated they use journal articles, phone application Omino®, Cochrane,

Medline®, RCH resources, Wito Rocket book of hospital care, Guidelines and IAP textbook of paediatrics.

Question 13. Please provide any additional comments, recommendations, or general or specific feedback about the STG topics that we should cover for the next update:

No comments as I have not seen access to this
None
There should be a separate STG for paediatrics alone
Please provide references from which Guidelines have been based on
Warfarin protocol so that INR testing can be done at Sub-divisional level
Easily accessible soft copy STGs
Development of neurological guidelines

Prescribers recommended references be provided in the STGs, warfarin protocols, easily accessible soft copies of STGs, paediatric STGs and neurological guidelines for the next STG update.

Limitations

This study provides an insight into meropenem use at CWMH, however, there is the potential for error in several aspects of the study. Many of the *Restricted Antimicrobial Request Forms* were incomplete with omitted data. Furthermore, not all microbiology data could be found in the specimen record books (despite having two data collectors double checking the record) and not every patient could be found on PatisPlus® dispensary records due to illegible or missing patient numbers (NHNs) on the *Restricted Antimicrobial Request Form*. The quantities of unknown data are shown in Table 1.

Table 1. Quantities of unknowns in the DUE

Data area	Quantity of unknowns
Patient age	2 (2.3%)
Patient ward	4 (4.5%)
Indication	3 (3.4%)
Length of therapy dispensed	7 (8%)
Previous antibiotics	6 (6.8%)
Laboratory efficiency	27 (27%)
Microbial culture results	13 (11.6%)

Limitations of the Prescriber Survey included the small number of respondents to the survey from a small range of specialities which could lead to bias of the results. Some of the multiple choice answers used were found to lead the respondents resulting in responder bias.

Discussion

This report is assessing the appropriate use of meropenem according to the *Indications for Meropenem Use at Divisional hospitals Policy*. Factors affecting the use of meropenem include:

1. The effectiveness of infection control and prevention measures
2. Availability of CWMH's hygiene practices and facilities
3. The efficiency of the microbiology laboratory and dissemination of results
4. Appropriate prescribing of antibiotics
5. Use of Policies and Standard Treatment Guidelines
6. Stock management of essential medicines and consumables
7. Utilisation of PatisPlus® in Pharmacy and Microbiology departments

8. Pharmacist's clinical monitoring of meropenem usage
9. Communication between hospital departments and systems of information sharing.

INFECTION CONTROL UNIT NURSES

On 12 February 2015, the Infection Control Unit nurses were interviewed. The Infection Control Unit consists of two nurses and a sister. When asked what their role at the hospital is, the nurse produced her position description which stated that the primary purpose of an infection control nurse is to be 'responsible for the overall co-ordination, implementation, facilitation and monitoring of the infection prevention and control program in CWMH.'

The position description also outlines interpersonal relationships with the Microbiology laboratory supervisor and staff, heads of the clinical departments, head of support services and members of the CWMH Infection Prevention and Control Committee.

When the microbiology laboratory reports a multi-resistant organism case to the infection control unit, the nurses follow-up on the case and write a management plan in the patient notes including personal protection equipment to be used, hand hygiene and barrier nursing or isolation measures.

Outbreak

An outbreak is declared when the Microbiology department reports two or more cases in the same ward with the same organism and the same resistance pattern. During an outbreak, hospital equipment is monitored for infectious organisms and a management plan including hand hygiene, screening all patients in the ward (e.g. rectal swabs) and closing the area is written and implemented for the affected ward.

A detailed report of each outbreak is written by the infection control sister and then distributed to the risk management officer and medical superintendent. The report is then presented to the infection control committee which meets each month. This committee is chaired by the Medical Superintendent and includes all departments such as Pharmacy, Microbiology, ICU, Dental, Surgical, Medical and Emergency and the heads of the wards.

The distribution of patient age in Graph 2 correlates to 2 outbreaks in NICU, another in PICU and one outbreak in the adult ICU during the study period. All of these outbreaks were due to *Klebsiella Pneumoniae* (ESBL).

Despite the infection control nurses reporting that a ward is closed with no patients entering and exiting if there is an outbreak, seven (8%) patients prescribed meropenem and so having a multi-drug resistant organism, were moved from one ward to another potentially spreading infection. It is recommended that every case of a multi-resistant organism be treated as an outbreak in order to prevent movement of patients and spread of infection leading to the development of antibiotic resistance and increased costs to the healthcare system. (1)

Gold Standard

The SENIC study on efficacy of infection control determined that nosocomial infection rates reduced by 32% if the following were present:

1. A balance between surveillance and control efforts
2. At least one full time infection control nurse per 250 beds
3. A trained hospital epidemiologist and
4. For surgical wound infections, feedback of wound infection rates to practicing surgeons (2).

Officially CWMH has 508 beds however this does not include clinics and outpatient services. Although CWMH has sufficient infection control nurses according to these recommendations, it is important to note that the infection control nurses are not focused solely on infection control as they are also responsible for waste management and cover staff shortages in other areas of the hospital. It may not be practical due to funding for CWMH to have a full-time epidemiologist. Seeking assistance from epidemiologists is recommended, with WHO a possible source for this help.

The Ministry of Health published the *Infection Control Manual for Health Facilities* in 2002 and this is used as a guide by the infection control unit nurses. The manual includes infection prevention, hand hygiene, cleaning, wound dressing, waste disposal, medicine preparation and staff health among other topics. However, key topics such as staff uniform, outbreak control and patient isolation procedures are not included. As key topics are not included and the manual is more than 10 years old, it is recommended that the manual be updated.

Surveillance

An important factor in controlling *KPN (ESBL)* and *E.coli (ESBL)* is awareness that they are abnormal pathogens and should trigger immediate action of microbiologists, infection control staff and ward staff to rapidly isolate and use contact precautions in the ICUs. The use of active surveillance methods to identify cases should be performed including taking cultures of asymptomatic patients (rectal swabs) housed in the same wards as patients who are infected with multi-drug resistant organisms (2). This part of surveillance is already being carried out by the Microbiology and Infection Control Unit. It is suggested due to the frequency of outbreaks at CWMH that swabs of equipment be taken regularly to monitor for reservoirs of infection. The implementation of active surveillance methods requires further investigation at CWMH.

Reservoirs

The sharing of ventilators was pin pointed as the source of infection last year in the NICU and PICU leading to the spread of a meropenem resistant *Acinetobacter baumannii* strain. The cause of this outbreak was due to the reusing of ventilator tubing, insufficient autoclaving and cleaning processes. The nurses stated there is now an effort to avoid sharing ventilators however this is not practical due to insufficient numbers of ventilators at CWMH. Unfortunately, there is no funding currently available to purchase new ventilators. According to FPBS the cheapest approved ventilator costs approximately \$US27,000. Ideally, the infection control unit has recommended that each ward should have their own ventilator. There is an urgent need to review the cleaning and autoclaving process for medical equipment.

Staff uniforms are another potential reservoir of infection. Whilst visiting the wards, some of the nurse's caps were visibly soiled and it was noticed that many nurses were constantly touching them whilst caring for patients. The infection control sister reported that nursing staff launder their own uniforms including their caps and there is currently no protocol for staff uniform washing (e.g. after every shift). She stated that most nurses only wash and starch their cap when it is visible soiled.

We recommend a policy be developed regarding uniform laundering and the nurses caps and uniforms be swabbed and investigated as a potential reservoir of infection and caps possibly removed from the uniform. A comprehensive study published in the Infection Control and Hospital Epidemiology journal has shown that neck ties and long sleeves are a reservoir for infective organisms and lead to increased rates of nosocomial diseases. Wrist watches, nurse caps and lanyards are also potential infection reservoirs (3).

Infection control training

Staff training on infection control and prevention is only completed once or twice per year and other in-house training is carried out weekly or fortnightly due to limited staff in the infection control unit and minimal resources. Staff training for hand hygiene should be done regularly with or without an outbreak (4). There were no protocols for hand hygiene audits or audits on the availability of antibacterial hand gel, soap or paper towel for the wards. The infection control unit nurses stated that paper hand towel is commonly in short supply in the hospital and has pinpointed shared or reused hand towels as a potential source of infection. In addition, during the data collection period, there was a lack of soap and paper towel in both patient and ward staff toilets throughout CWMH.

When asked what was needed to improve infection prevention and control the nurses said there were supply issues with basic consumables such as paper towel. Therefore, in light of this information, it is recommended that hand hygiene audits and availability of hand hygiene commodities be carried out monthly in all bathrooms and ward hand washing stations. Better communication between nursing staff and hospital cleaning staff to ensure soap and paper towel are refilled daily is recommended.

By implementing the infection control recommendations stated above, CWMH will have a greater chance of preventing nosocomial multi-resistant infections and outbreaks and thus, the need for meropenem will reduce as will the risk of developing antibiotic carbapenem resistance.

ICU WARD NURSES

On 6 December 2014 the ICU, PICU and NICU were visited to investigate hygiene and infection control practices as these wards had the highest number of patients on meropenem during the study period.

Adult ICU

During this period, the adult ICU was under renovation and was being housed in half of the Cardiac unit which is not ideal for infection control. The new ICU is said to have isolation units for patients infected with multi-resistant organisms, this is important to prevent infection spread.

NICU and PICU

It was found that the sisters in charge of NICU and PICU were very proactive in infection control ensuring all staff and visitors washed their hands before entering, with clear marked lines on the floor indicating 'clean' areas and there were posters explaining when to wash hands (the WHO 5 moments – Appendix 6) and correct hand washing technique. They also explained the protocol of one-to-one nursing during an outbreak to avoid spread of infection. The nurses only wear gloves whilst performing a medical procedure and not during everyday care of patient. The PICU and NICU were found to have comprehensive hand hygiene measures to avoid infections, however, it is recommended that gloves be worn when there is a potential of highly infectious organisms such as in an outbreak. Appendix 7 depicts when gloves are recommended according to the World Alliance on Patient Safety and the WHO. It is recommended that staffs are familiar with the Guides and follow them. It was stated that one-on-one nursing was practiced during outbreaks; however, in reality this is impossible due to staffing constraints. It is recommended that more staff be made available to provide one-to-one care during outbreaks to prevent further spread of infection. The recommendations regarding ventilators can be found under the *Surveillance / Reservoir* section above.

There are concerns that specimens are not being taken before antibiotic therapy has begun leading to negative growth laboratory results. It is recommended that specimens are taken before therapy has begun and taken to the laboratory as soon as possible to ensure timely results. Nurses or other

ward staff should check their ward's pigeon hole at the laboratory at least twice per day. It is recommended that nurses question prescribers on whether a specimen has been sent before administering antibiotics.

MICROBIOLOGY LABORATORY

The head of the Microbiology laboratory was interviewed on 12 February 2015. The Microbiology laboratory has 9 staff and process approximately 150 samples per day. The time the laboratory receives the samples to the time the results are released takes 3-4 days.

Initially, samples are given to the laboratory reception and are entered into the laboratory system. Details such as ward, patient name and number, sample type and clinical information are attached to the samples. From the reception area the samples are collected by microbiology staff several times per day. The samples are cross checked with the computer system to ensure all the samples are accounted for. The patient name, unique patient number and ward are then entered into the appropriate sample type register. Depending on the specimen type, the sample will be cultured and then incubated overnight. Urine samples are checked for cells first and only incubated if cells are found.

The next day organisms are isolated and tested for sensitivity against an antibiotic panel. Each sample type has a different panel of sensitivities to test. There is no system for prioritising samples as all specimens are considered urgent. However, for ICU patients, the ward is phoned and notified of positive results. The infection control unit is notified of all cases of multi-resistant organisms.

Results are recorded in the registers and then transcribed onto the yellow results slips and signed off by the head of the laboratory. These yellow slips then go into the ward pigeon hole at the laboratory reception. The phlebotomists also occasionally take the yellow results slips to the wards. The laboratory reception is open 24 hours a day, 7 days a week and the Microbiology laboratory can be accessed by doctors after hours.

If a blood sample is found to be negative after 48 hours, the samples are incubated for 7 days or for 14 days in endocarditis cases. This is a potential reason for some results taking more than a week to be reported.

There is a computer system available and used by the other laboratories however it is not used by microbiology because they cannot generate resistance statistics from the program. The head of the laboratory would like to use a computer system if this was possible.

Sensitivity testing

The sensitivity test is performed when a culture is found positive. All of the sensitivities in the panel are tested and reported for every sample. The head of Microbiology department was concerned that the panels contain antibiotics no longer used at the hospital and some newer antibiotics which are being used at CWMH are not being tested. Colistin is a recent new addition to the testing panels; however, it was being used clinically at CWMH before the Microbiology department had access to the sensitivity testing panel.

It is recommended to remove the antibiotic testing panels for antibiotics which the hospital no longer uses. In addition, when a new antibiotic is being introduced to the hospitals, it is highly recommended that the testing panels are also made available to the Microbiology laboratory to ensure rational use of antibiotics.

Microbiology laboratory efficiency

Graph 11 measures the time between prescribing and dispensing of meropenem for each patient. Limitations to this data are the date the *Restricted Antimicrobial Request Forms* were signed was often left blank; therefore, it was assumed that the date of the specimen for sensitivity was taken was when the form was filled out. According to the infectious disease prescriber, doctors really pay minimal attention to what information we write on this Form, it's a formality to get the drug we want / need. Therefore, the use of the *Restricted Antimicrobial Request Forms* for this purpose is limited.

The date therapy was initiated was taken from the dispensing records on PatisPlus®. Dispensing entries are not recorded if the internet is not working. Therefore, if the internet was down on the day meropenem therapy was initiated; the length of therapy may be longer than stated in this report.

The *Indications for Meropenem Use at Divisional Hospitals Policy*, states that the treatment unit must submit a completed request form with microbiology results attached. In the case of an outbreak, empirical therapy can be administered for a maximum of 72 hours whilst waiting for the microbiology results. If the specimen takes 72 hours, which it does, according to the head of the Microbiology department; then in theory, it should not take longer than 4 days between the form being filled and the medication being dispensed. However, the time between prescribing and dispensing was more than 72 hours in 45% of cases and 6 cases were more than 2 weeks. Possible reasons for these finding include poor communication between the laboratory and prescribers or delays in laboratory procedures.

The results of laboratory efficiency (Graph 13) may be biased towards a shorter time frame. Negative results found in the laboratory books were stamped as no growth in 48 hours, so these results were assumed to be recorded in 48 hours. Positive results which are more important for the use of meropenem generally took longer. Of the 64 results that had a correctly recorded time line (not unknown or reporting error); 21 (33%) of cases took longer than 72 hours. The 'reporting error' results emphasise the error in the current reporting and recording of results. The number of unknown and reporting error results diminishes the significance of the laboratory efficiency results.

When sensitivity results are released from the laboratory showing a need for meropenem or any other antibiotic, therapy should be initiated as soon as possible. Graph 12 shows the majority of meropenem cases were initiated 3 to 4 days after the results became available. This shows a need for laboratory results to be more accessible to prescribers and other hospital staff, possibly by recording results on PatisPlus® instead of in the paper records. Using PatisPlus® could also reduce error due to potential misinterpretation of hand written laboratory results and data discrepancies in laboratory results recorded on the form compared to the laboratory record books.

In addition, the inpatient pharmacist stated the pharmacy intern is sent to the laboratory every day to follow up on restricted antibiotic use results and it takes them more than one hour. This is not surprising, whilst searching the laboratory records for the data for this study, it took 2.5 days for two data collectors to look for 67 results. That is, it took approximately half an hour to find each result. Some results could not be found with 13 unknown culture results. The time it took for the specimen to be processed by the laboratory is unknown for 27% of the specimens due to poor recording of the specimen being taken or poor recording of the results being published.

It is recommended that the microbiology laboratory sensitivity results be entered into the PatisPlus® computer system which will prevent missing results and hand written errors as well as save time by reducing paperwork and making recording results more efficient.

If PatisPlus® is to be used, it is recommended that the Microbiology department be trained on how to use the program but also how to generate sensitivity pattern reports. The head of the Microbiology department stated the reason for not using PatisPlus® was due to the system's inability to generate these reports and therefore, it is highly recommended that the PatisPlus® Remediation Project Steering Committee be consulted to see if this is possible to program in PatisPlus® or to develop a user-friendly, efficient system for this reporting.

The head of the Microbiology laboratory department believes the laboratory efficiency would be improved by more staff, more computers and an appropriate computer system. It is recommended that the PatisPlus® Committee provide training and assistance to the laboratory staff during the process of moving from paper to computer records.

Microbial culture results

From Graph 14, the most common organism found in patients was *Klebsiella pneumonia* (KPN) with and without (ESBL). This organism was responsible for all four outbreaks in the study period. *Acinetobacter baumannii* had the greatest meropenem resistance problem. Thirteen (12%) of the culture results were unknown as they were not reported on the *Restricted Antimicrobial Request Form* and could not be found in the laboratory record books. This information points to a need to update the system for reporting microbiology results by using PatisPlus® to electronically record results and thus increases accessibility to prescribers, ward staff and the Pharmacy department.

By implementing the recommendations stated above, the efficacy of the Microbiology laboratory department will be increased which will allow patient specimens to be processed faster and more accurately, resulting in prescribers initiating correct treatments faster which will give better prognosis for the patients but will also reduce antibiotic resistance and reduce the high consumption of meropenem at CWMH.

PRESCRIBERS

An infectious disease prescriber was consulted via email regarding the prescribing practices for meropenem and any issues they think are contributing to the high utilisation of meropenem. Their recommendations have been added to various sections of the report.

Surgical wound infections and urinary tract infections

According to Graph 3, the acute surgical ward (ASW) had the second largest number of patients treated with meropenem (patients with multi-resistant bacteria). It is understood that the acute surgical ward has high care facilities second only to ICU and not all patients in this ward are surgical patients. The high number of multi-resistant bacteria cases in ASW may be due to transfer of infectious patients from ICU.

As per the SENIC study mentioned above, it is recommended that for surgical wound infections, feedback of wound infection rates to practicing surgeons to be completed to help surgeons increase infection control practices. There were two patients on meropenem due to surgical wound infections in the study period.

From Graph 4, 15% of the patients studied required meropenem for multi-drug resistant urinary tract infections this highlights an area that needs to be investigated further by the Infection Control Unit.

Appropriate Prescribing

The Australian Electronic Therapeutic Guidelines (eTG) recommends prescribers follow the antimicrobial creed when prescribing all antibiotics (5).

The antimicrobial creed (Box 2.1)

M	microbiology guides therapy wherever possible
I	indications should be evidence-based
N	narrowest spectrum therapy required
D	dosage individualised to the patient and appropriate to the site and type of infection
M	minimise duration of therapy
E	ensure oral therapy is used where clinically appropriate

Empirical Treatment

As seen in Graph 12, six patients were treated empirically before microbiology results became available. According to the meropenem policy, empirical treatment should only be administered for a maximum of 72 hours before laboratory results are known. Therefore, the patient started on meropenem 13 days before and another a week before sensitivity results were known, were not following the Policy nor were they following the antimicrobial creed.

Specimens taken BEFORE initiation of therapy

It is important that the first dose of an antibiotic is not given until a specimen is taken. According to the infection control nurses, a specimen is not always taken before antibiotic therapy is initiated but they always test after the course to ensure no growth.

Regardless of whether an organism with sensitivities has already been confirmed, a blood culture and other relevant body fluids should be taken immediately before meropenem therapy is initiated according to the *Indication for Meropenem Use Policy*. Based on Graph 8, the Policy was only adhered to in 32.3% of cases. However, there is the potential for bias as specimens may have been taken at another time and not recorded on the *Restricted Antimicrobial Request Form*. The lack of appropriate samples may be due to lack of knowledge of the *Indications for Meropenem Use at Divisional Hospitals Policy* and reinforces the need for the policy to be updated, promoted and made available on the intranet. Without appropriate microbiology results to confirm the need for meropenem, patients are put at risk of developing carbapenem resistance. Carbapenem exposure is the single most important risk factor for developing carbapenem resistant enterobacteriaceae such as *Klebsiella pneumonia (ESBL)* (1). Rationally prescribing meropenem will help to prevent the development and spread of resistant organisms.

Restricted Antimicrobial Request Form

On the top of the *Restricted Antimicrobial Request Form* it states, 'This form must be completely filled before sending down to the pharmacy,' however, the Form was not completed correctly for many of the cases. As mentioned above, according to the infectious disease prescriber, doctors really pay minimal attention to what information we write on this Form, it's a formality to get the drug we want / need. The indication was not clear in many cases and no indication stated in 3% of cases. Culture results was stated as an indication for 59% of all cases (Graph 4), however, this is not enough information for the pharmacy staff to accurately assess if the dose prescribed is appropriate. A limitation of this data is that in many cases more than one form was completed as therapy was

extended, the information from each of these forms was not analysed individually and therefore individual forms may have been less comprehensive. Consultants are commended for signing every *Restricted Antimicrobial Request Form* during the study period (Graph 10), however, in light of the above findings; it is recommended that they read the content of the form thoroughly before signing in the future. In addition, the Pharmacy department need to increase their scrutiny of the Forms before dispensing.

It is unclear based on the *Restricted Antimicrobial Request Form* which patients are part of the defined clinical outbreaks and which are not. It is recommended that the form include tick boxes indicating if the patient is affected by an outbreak or not as the Policy for meropenem use differs for patients affected by an outbreak. To allow the Pharmacy department to quickly and easily get in contact with prescribers should they need to query a *Restricted Antimicrobial Request Form*, a mobile contact number section is recommended to be put on the updated Forms.

It is highly recommended that a review of the *Restricted Antimicrobial Request Form* be conducted at CWMH in consultation with the clinical medical team and pharmacy (with the possible formation of an antimicrobial stewardship team). When a new Form is developed, the importance of the Form should be widely disseminated with awareness sessions conducted aimed at both the prescribers and Pharmacy department – prescribers to fill in the form correctly and understand its clinical importance and the Pharmacy department to monitor the new Form to maintain its clinical relevance.

Meropenem Dosing

According to the inpatient pharmacist, prescribers mainly use the Australian Medicines Handbook (AMH) and Frank Shann's Drug Doses (a paediatric dosing reference from the Royal Children's hospital in Melbourne) for meropenem dosing as the dosing information is not available in the Fijian Antibiotic Standard Treatment Guidelines.

Using the AMH and eTG clinical references, many patients were under dosed with meropenem as seen in Graph 5. It is important to note that not all data for every patient was available from the form to fully assess whether the dose is appropriate. Graph 5 shows 34% of patients were prescribed 500 mg IV, TDS which according to the eTG is only appropriate for urinary tract infections (5). However, only 15% of patients had UTI listed as an indication (Graph 4) and many of these were children, meaning at least 19% of patients were dosed incorrectly with this dose alone. According to the eTG, for adults with normal renal function for sepsis, the recommended dose is 1 g TDS (5). Only 15% of adult patients with sepsis received this recommended dose.

For meningitis the recommended dose is 2 g TDS or 40 mg/kg for children. One 3 month old was given 10 mg/kg for meningitis and there was no renal function information given. A 24 year old female who developed meningitis was given 500 mg BD then changed to TDS which is just 25% of the recommended dose and even with a GFR of less than 10 mL/min the recommended dose is still higher than that prescribed. Another meningitis patient was given 30 mg/kg. Alarming, none of the meningitis cases were dosed as per the *Australian Electronic Therapeutic Guidelines*.

The weight of the patients prescribed 30 mg BD and 60 mg BD were not recorded, therefore these paediatric doses cannot be assessed based on recommended dosing. For several patients, renal failure was recorded and appropriate dosing was given.

Also, it is recommended that the *Indications for Meropenem Use at Divisional Hospitals Policy* be updated to include more specific indications as well as recommended dosing for each indication as the current Fijian *Antibiotic Guidelines 3rd Edition 2011* does not include meropenem. The

information given on the *Restricted Antimicrobial Request Form* should also be updated to ensure it contains enough information (renal function, weight, appropriate indication) for the pharmacists to confidently approve the therapy as appropriate.

Length of meropenem dosing

According to the findings in Graph 6 and 7, the length of therapy prescribed for meropenem varied greatly from a STAT dose to 42 days. The length of therapy dispensed on average was shorter than that prescribed. Reasons for this could be; internet problems in the inpatient pharmacy leading to dispensing records not being recorded in PatisPlus®, the patient become deceased or therapy discontinued before the patient received all prescribed doses. There is potential for bias as 8% of patients could not be found on PatisPlus® and their length of therapy dispensed is unknown.

According to the Antimicrobial Creed, the length of antibiotic therapy should be as short as possible to control infection. Recommended length of therapy in the eTG varies according to the indication and the shortest stated period of use is 14 days. For meningitis it is recommended to treat for 14 days after the last positive culture result (5). The patient prescribed meropenem for 42 days had meningitis.

One patient was given a STAT dose of meropenem which is not evidenced based practice. Meropenem is a beta lactam antibiotic so requires a sustained concentration over a period of time to effectively kill bacteria. There is no evidence of benefit from a STAT dose and this practice may lead to antimicrobial resistance (1). It is recommended that STAT doses of meropenem are not prescribed to avoid the development of antibiotic resistance.

The Meropenem Policy does not advise on the length of therapy. It is recommended the updated Policy should include evidenced based recommended lengths of therapy for each indication. In addition, the recommended *Fijian Antibiotic Therapeutic Guidelines for Meropenem* should be made available on the Ministry of Health website and the hospital intranet to ensure all prescribers have access to standard treatment guidelines. An awareness campaign in collaboration with the Medical Clinical Services Network is also highly recommended to disseminate the new Guideline, Policy and restricted antibiotic Form.

Previous antibiotic therapy

According to Graph 9, approximately 13.6% of patients studied were not dispensed any other antibiotics previous to meropenem. This may be inaccurate as only 38.6% of cases had previous antibiotics recorded on the *Restricted Antimicrobial Request Form*. The antibiotics most commonly tried before meropenem were; ceftriaxone, ciprofloxacin and metronidazole. A limitation of this data is that at least 48% of patient's *Restricted Antimicrobial Request Forms* had incomplete information in the 'previous antibiotics tried' section. Considering the underutilisation of this section of the form and the availability of this data in the patient file and dispensing program, the necessity for the 'previous antibiotics tried' section should be reviewed. The section is however important in circumstances where the microbiology results show sensitivity to meropenem and another more appropriate antibiotic and this antibiotic has already been tried without success or is out of stock.

Sensitivities guiding prescribing

As shown on Graph 15, of the 88 patients studied, there were 33 (38%) of cases where the patient specimens were found to be sensitive to another antibiotic other than meropenem and amikacin, yet all but one were given meropenem and only 6 patients were given meropenem empirically before the results became available. In fact, in some of these cases, the organism identified was not even sensitive to meropenem. It was found that in many of these cases, the organism was sensitive

to chloramphenicol as well as meropenem and amikacin, however, chloramphenicol was out of stock for the entire study period due to product safety concerns.

There are potential biases in these results as the full patient histories were unknown and the data on other antibiotics tried is incomplete. In many cases no reason was given for using meropenem instead of a narrower spectrum alternative chloramphenicol and it was later found that this antibiotic was out of stock for the entire study period.

In some cases, the patient grew multiple organisms and required meropenem as well as other antibiotics. There were several cases where the organism was not sensitive to any antibiotic including meropenem however, meropenem was still prescribed. A treatment guideline for patients with resistant organisms is recommended to be developed.

Key recommendations from the *Outbreaks of Carbapenem-Resistant Enterobacteriaceae* report are:

1. The Antibiotic order must include dose, duration and indications; without a duration and indication, it becomes very hard for other clinicians to change or stop the antibiotics because they don't know why the patient was taking them in the first place or how long they were supposed to be on them
2. Getting the right cultures before therapy is started
3. When empirical therapy is used have an 'antibiotic pause;' after 72 hours of therapy, reassess therapy, look at susceptibility results and see if therapy can be narrowed, it's a good time to make a diagnosis and put down a therapy duration (1).

By implementing the recommendations stated above, patients will receive the correct effective antibiotic in a timely manner thus increasing patient prognosis and decreasing the risk of antibiotic resistance, reducing the clinical need for meropenem therefore reducing the high consumption at CWMH (Graph 1) and preventing the development of carbapenem resistant bacteria.

Prescriber survey – Meropenem Policy and Restricted Antimicrobial Request Form

The doctor survey results are subject to bias as only a small sample of doctors (13 prescribers) responded to the survey compared to approximately 25 consultants and 40 registrars who were involved in completing the *Restricted Antimicrobial Request Forms* between October 2013 and October 2014.

More than half of the prescribers were registrars at CWMH. The other prescribers interviewed were 4 consultants and 2 medical officers. Seven respondents specialised in the Paediatric department, with 3 Internal medicine prescribers and 2 Medical officers. As the *Meropenem Use at Divisional Hospitals Policy* was developed in 2008 and as more than half of the prescribers are registrars, this may have accounted for 5 of the respondents stating they were unaware of the Policy. In addition, their lack of awareness of the Policy may have been a factor contributing to the inappropriate prescribing of meropenem at CWMH.

This question also highlights that the Policy requires updating and an awareness campaign regarding the use of meropenem may be long overdue. Two respondents did not have access to the Policy which highlights the need for the Policy to be added to the CWMH intranet to increase its awareness and usage amongst prescribers. Of those respondents who were aware of the policy, the majority stated they were an invaluable resource and were reassured to know if it is there. This question could have led prescribers and is likely to be affected by responder bias.

All prescribers were aware of the *Restricted Antimicrobial Request Form* and all stated they use the form every time they prescribe meropenem. This question is also subjected to responder bias due to

the wording of the second question. However, as meropenem is a restricted antimicrobial agent listed on the Essential Medicines List, the pharmacy should request the prescriber to fill in the form every time meropenem is charted. As found during the meropenem data collection, the Forms are being completed by the prescribers, but not necessarily before meropenem is dispensed by pharmacy. Again, awareness of the protocol stated in the Policy and adherence by the prescribers plus the Pharmacy department enforcing this protocol before dispensing is highly recommended.

Prescriber survey – Standard Treatment Guidelines

Twelve prescribers stated they had access to the Fijian Standard Treatment Guidelines with 11 prescribers having access to the Antibiotic Guidelines. However, it is noted that meropenem is not stated in the current Antibiotic Guidelines, therefore would not help the prescribers to accurately prescribe this restricted antibiotic.

As Guidelines take a very long time to develop, it is unreasonable to publish them every time a new medicine is added to the Essential Medicines List. Therefore, it is highly recommended that the guidelines be made available online. Following correct essential medicines policy procedures, all medicines added onto the EML should be accompanied by a Therapeutic Guideline to provide guidance to clinicians of what health condition to use it and what dose and duration to prescribe. This also allows the quantification and prediction of medicine usage for FPBS procurement, insuring availability of the medicines at all times and leading to reductions in out of stocks. Each time a new medicine is added onto the EML, an amendment to the therapeutic guideline will be made available online with circulations to all hospital staff alerting them to the new change.

Most of the prescribers had access to the STGs, however, prescribers should have 100% access to all STGs at all times. It is recommended that an awareness campaign be conducted to increase awareness and distribute hard copies of the Guidelines to all prescribers in Fiji. As the prescribers were based at Suva's CWMH, their access to Guidelines may be increased compared to other areas of Fiji where the Guidelines are hard to come by or aren't distributed. In addition, the Guidelines should be made available online in electronic form to increase their accessibility to prescribers. This will also increase the access to prescribers. However, it is still recommended to distribute hard copies as many clinicians may not have access to reliable internet or computers.

Ten prescribers used the Guidelines in their practice and most respondents stated they were reassured to know the Guidelines were there with some stating that they are an invaluable resource, thus indicating that the STGs were recognised as an important reference tool in the practice of CWMH prescribers. It is important to note the multiple choice answers to this question were leading as they had two parts to their answers which may not have given prescribers an opportunity to answer truthfully.

Clinical topics prescribers would like covered in the STGs include; neurological disorders, stroke, epilepsy, endocrine, rheumatology and paediatric specific guidelines. These suggestions will be forwarded to the Medical Clinical Service Network to consider for developing the next set of Guidelines. Electrolyte imbalance was stated, however, guidelines for this therapeutic area are stated in the *Emergency Drug Guidelines, 2nd Edition, 2008*. In addition, warfarin protocols to allow INR testing at subdivisional level, DVT and anticoagulation were also therapeutic areas in which the prescribers highlighted weren't covered in the current STGs. The new *Cardiovascular Therapeutic Guidelines*, due to be published later this year, will cover these topics in detail and will be launched around the country. In addition, a comment was made to provide references from which the Guidelines have been based on. The new Cardiovascular Guidelines uses references throughout the document and lists a full reference list for the users. This format is highly recommended to be used for the new STGs in the future.

When prescribers were asked what other resources they refer to for management of STG conditions, online clinical databases such as Medscape® and Up-to-date® and other online resources were popular with clinicians. Therefore, this may indicate if the STGs were to be placed online, prescriber access and uptake may increase. In addition, one prescriber asked for easily accessible soft copies of STGs.

These recommendations highlight the importance of promoting and disseminating the Policy, Restricted Antimicrobial Request Form and prescribers having access to reliable clinical resources as all of these resources are essential for prescribers to prescribe meropenem judiciously without creating antibiotic resistance and to improve the clinical outcome of the patients at CWMH.

PHARMACY DEPARTMENT AND FIJI PHARMACEUTICAL AND BIOMEDICAL SERVICES (FPBS)

PatisPlus® Internet Connection

It is noted that the dispensing data may be open to bias. When the internet is not connected to PatisPlus®, the dispensing system is unable to function properly resulting in medication dispensings not being recorded. Therefore, many dispensings may be missing from the program's history.

It is highly recommended that the PatisPlus® Remediation Project Steering Committee and the Information Technology Department of CWMH work together to solve the problem of internet outages and how to alter the program to work offline; or to use a back-up system to save the data entered whilst offline and re-submit when an internet connection is available.

Clinical monitoring of meropenem usage

As described above in the Prescribers Section, a large percentage of meropenem patients were under-dosed when compared to the dosing and indications in the Australian Medicines Handbook (AMH) and Australian Electronic Therapeutic Guidelines (eTG). It is recommended that CWMH pharmacists are encouraged to be more vigilant when clinically screening all *Restricted Antimicrobial Request Forms* and to double check the dosing with the AMH or eTG (until the new Meropenem Guideline is developed) to ensure the dosage prescribed is appropriate for each patient.

Unfortunately, the latest edition of the Fiji Antibiotics Guideline does not have meropenem listed. It is suggested that the Medical Clinical Service Network (CSN) in consultation with the Pharmacy department, develop the Meropenem Guideline to ensure all prescribers and pharmacists are aware of the indications and approved dosages of meropenem in Fiji.

Pharmacists are also recommended to double check the sensitivity results of laboratory specimens to ensure the request antibiotic is appropriate for the patient. It is understood that this is very time consuming for the inpatient pharmacy, however, with the recommendation of the Microbiology department using PatisPlus® to record the sensitivity results, this should make the process of finding patient results easier and therefore, ensure the correct screening of antibiotic requests by the Pharmacy department.

In addition, empirical treatments were found to exceed the 72 hour limit stated in the Policy. Meropenem should be monitored and pharmacists are recommended to follow-up with prescribers and microbiology sensitivity results to ensure empirical use does not exceed the 72 hours stated in the Policy.

The length of therapy of meropenem varied greatly and the current Policy does not state a recommended length of therapy. As mentioned previously, a new Meropenem Guideline is

recommended to be developed which should include recommended lengths of therapy for each indication of meropenem and which is highly recommended to include an antibiotic pause, which is a concept designed to make prescribers reassess the patient (re-order more sensitivity tests) at specific time intervals before more antibiotic can be dispensed (1). A force function (every 7 days) is recommended to be built into the dispensing software of PatisPlus® to ensure a reason for dispensing restricted antibiotics is entered into the computer system and recorded before allowing the dispenser to proceed. This will help to alert pharmacy staff of any long term restricted antibiotic use (1).

The *Restricted Antimicrobial Request Forms* used for this DUE were poorly completed with missing data from the indication, incomplete culture results, dates omitted and specimens taken sections left blank. To avoid incomplete forms, it is recommended that the documents be carefully checked by the pharmacists to ensure all parts are correctly completed. Therefore, the pharmacy has all of the correct information to make well informed clinical decisions on the correct dose and indication for each patient. An updated *Restricted Antimicrobial Request Form* is highly recommended to be developed to make the Form more user friendly for both prescribers and the Pharmacy department and to reduce crucial clinical data being omitted.

To ensure the request forms are screened clinically (ensuring correct doses are prescribed), it is recommended that sufficient pharmacy staff be made available to allow inpatient pharmacists sufficient time to review all restricted antimicrobial request forms, access microbiology sensitivity results and contact prescribers if necessary. Electronic or hard copy access to recent editions of the AMH and eTG is essential for all pharmacists to clinically screen antimicrobial requests accurately.

According to the International Pharmaceutical Federation (FIP) *Statement policy – control of antimicrobial medicines resistance (AMR)*, the FIP encourages pharmacists to:

- provide proper counselling and appropriate written information when dispensing antimicrobials
- work with prescribers so that dosages prescribed are sufficient for the completion or continuation of a course of therapy
- provide updated information on antimicrobial medicines to prescribers as well as health-care professionals who administer or otherwise influence the use of medicines
- be actively involved in matters of hygiene and infection control in all health-care settings and
- effectively monitor the supply and use of antimicrobials by their patients (6).

Antibiotic out of stock issues

During the study period CWMH Pharmacy reported the following antibiotic injections out of stock: chloramphenicol 1 gram, ceftriaxone 1 gram and 250 mg, Cephalothin 1 gram, erythromycin 1 gram, ciprofloxacin 100 mg/50 mL, penicillin G 1 mega unit, Ampicillin 500 mg. Table 2 shows the antibiotics out of stock at FPBS from October 2013 to October 2014. The 'Xs' represent times the antibiotics were out of stock. Chloramphenicol was out of stock for the entire study period however, this was due to unforeseen product safety concerns.

According to the CWMH Pharmacy department, currently there is no written protocol for when medicines are low or out of stock. When a particular item is low or out of stock, the Pharmacy department tries to restrict usage to vital departments only. In addition, depending on the level of distribution of an item, CWMH Pharmacy request excess stock from other health facilities in Fiji to be forwarded to CWMH Pharmacy. As a last resort medicines are procured from local suppliers for the hospital.

CWMH Pharmacy stock levels are checked routinely and FPBS is advised if they are running low on certain items. The usage report is completed yearly and not on a regular basis but the Pharmacy is

trying to complete usage reports regularly to ensure stock information reaches FPBS in a timely manner. Currently, the stock management software (EPICOR®) and PatisPlus® are not linked and only data from EPICOR goes to FPBS.

It is recommended that cases where antibiotic stock shortages have guided therapy be documented on the *Restricted Antimicrobial Request Form* and with the Pharmacy department to allow more accurate ordering based on demand not use.

The infectious disease prescriber stated that essential medicines being out of stock is so standard that it hardly seems worthy to report and prescribers all just despair. The problem of essential medicines such as antibiotics being out of stock is of great concern and is highly recommended to be investigated further.

In regards to the information above, it is highly recommended that written protocols are developed as soon as possible to ensure the correct procedures are followed in regards to medicines running low or out of stock. In addition, it is recommended that the information technology department at CWMH, FPBS and PatisPlus® Remediation Project Steering Committee collaborate and come up with strategies to link EPICOR® and PatisPlus® so the programs are able to communicate. Therefore, when a medicine is dispensed it automatically links to the stock management program and thus gives accurate usage data instantly. By linking the programs, this intervention will alert the stock management teams at both CWMH Pharmacy and FPBS in advance of stock which is running low so both departments are able to work together to obtain more medicine in a timely manner resulting in essential medicines being consistently available.

Table 2. Antibiotics out of stock at FPBS from October 2013 to October 2014. X = Out of stock

Dates	Chloramphenicol 1 gram injection	Cephalothin 1 gram injection	Ceftriaxone 1 g injection	Erythromycin 1 g injection	Ciprofloxacin 100 mg /50 mL injection
1 – 15 Oct	X				X
16 – 31 Oct	X				X
1 – 15 Nov	X				X
16 – 30 Nov	X		X	X	X
1 – 15 Dec	X		X	X	X
16 – 31 Dec	X		X	X	X
1 – 15 Jan	X		X	X	X
16 – 31 Jan	X		X	X	X
1 – 15 Feb	X			X	X
16 – 28 Feb	X			X	X
1 – 15 Mar	X			X	X
16 – 31 Mar	X			X	
1 – 15 Apr	X		X	X	
16 – 30 Apr	X				X
1 – 15 May	X				X
16 – 31 May	X				
1 – 15 Jun	X				
16 – 30 Jun	X				
1 – 15 Jul	X		X		
16 – 31 Jul	X		X		
1 – 15 Aug	X	X	X		
16 – 31 Aug	X	X	X		
1 – 15 Sept	X	X	X	X	
16 – 30 Sept	X	X	X	X	
1 – 15 Oct	X	X		X	
16 – 30 Oct	X				

Consumable out of stock issues

When visiting the ICU departments and the Infection control departments, the staff commented that there is often a lack of disinfectants, antiseptics and hand gel available on the wards. It is recommended audits investigating the availability of these consumables be conducted monthly in all wards to help pharmacy accurately record the consumption of these items to forecast the amount required for procurement from FPBS. Ward staff are also encouraged to report any items running low to the Pharmacy department to ensure pharmacy is able to obtain sufficient stock for the wards.

By implementing the recommendations stated above, clinical monitoring, dispensing accountability and stock availability will be increased. Therefore, patients will receive the correct effective antibiotic in a timely manner thus increasing patient prognosis and decreasing the risk of antibiotic resistance, reducing the clinical need for meropenem consequently reducing the high consumption at CWMH (Graph 1) and preventing the development of carbapenem resistant bacteria.

Summary of recommendations

The key recommendations for CWMHs departments are:

- Develop a strategic plan to aid in the implementation of the following recommendations
- Review and redevelop the *Indications for Meropenem Use at Divisional Hospitals Policy* and promote and disseminate the Policy to all prescribers and pharmacy staff
- Review and redevelop the *Restricted Antimicrobial Request Form* and promote and disseminate to all prescribers and pharmacy staff
- Develop a Meropenem Guideline and post on the hospital's intranet, Ministry of Health website and include recommended lengths of therapy as well as treatment guidelines for patients with completely resistant organisms
- The Medical Clinical Service Network will be forwarded a list of STGs and clinical topics suggested by prescribers
- In collaboration with the Medical Clinical Services Network, implement awareness raising interventions to ensure understanding of the new Guideline, Form and Protocol and thus increased compliance from prescribers
- Develop an antimicrobial stewardship team to implement rational use of antimicrobials practices and policies.

It is recommended that the Infection Control Unit:

- Treat all cases of a multi-resistant organism as an outbreak and reduce movement of infected patients between wards
- Seek assistance from an epidemiologist during outbreaks
- Update the *Infection Control Manual for Health Facilities* to cover staff uniforms and outbreak procedures
- Purchase more ventilators to avoid sharing between patients and wards and spread of infection and review the cleaning and autoclaving procedures for ventilators.
- Develop a policy on the laundering of uniforms
- Investigate nurse caps as a potential infection reservoir and potentially remove these from the uniform.
- Conduct hand hygiene audits and ensure availability of hand hygiene consumables such as soap and paper towel which should be refilled on a daily basis.

It is recommended that ward nurses:

- (Interventions may initially only be feasible to target nurses in the three ICU departments and ASW as these are the most critical areas for meropenem usage.)
- Ask prescriber on whether a laboratory specimen has been taken before administering antibiotics
- Ensure samples are taken before antibiotic therapy has begun and deliver samples to the laboratory as soon as possible
- Check Microbiology laboratory pigeon hole for results at least twice per day (whilst still using paper based system)

It is recommended that the Microbiology department:

- Record laboratory results on PatisPlus® instead of using paper based records. This will increase the efficiency of sensitivity results being made available to prescribers and thus result in prescribers initiating treatment promptly
- Obtain more computers to use PatisPlus® effectively
- Be trained on how to use PatisPlus® to enter in results and how to generate sensitivity reports.

It is recommended that prescribers:

- Receive feedback on their surgical wound infection rates
- Always take specimens before initiating antibiotic therapy
- Follow the antimicrobial creed
- Prescribe only according to recommended treatment guidelines (until the new Policy is developed – use the AMH or eTG).

It is recommended that the Pharmacy department:

- Document when out of stock antibiotics guide therapy
- Work with the IT department and the PatisPlus® Remediation Steering Committee to allow dispensing data to be recorded when the internet is down and then uploaded when the internet service returns
- Clinically screen *Restricted Antimicrobial Request Forms* and check doses against reliable resource such as the AMH and eTG
- Check microbiological sensitivities against therapy prescribed
- Ensure empirical therapy does not exceed 72 hours without review
- Develop written standard operating procedures for stock management, disseminate to all staff via training sessions
- Work with the IT department and the PatisPlus® Remediation Steering Committee to link the dispensing system PatisPlus® and stock management program EPICOR® so FPBS are able to track accurate medication usage in real time and thus help with usage predictions and stock management
- Audit consumables such as antiseptics and alcohol hand gel once per month and report usage data back to FPBS to reduce stock outages.

Conclusion

A drug use evaluation was performed investigating the high usage of meropenem at the Colonial War Memorial Hospital between October 2013 and October 2014. Data from the *Restricted Antimicrobial Request Form*, pharmacy dispensing program PatisPlus® and microbiology laboratory records were used to analyse the prescribing of meropenem compared to the *Indications for Meropenem use at Divisional Hospitals Policy* and treatment guidelines. Infection control unit nurses, Pharmacy department staff and the head of the Microbiology department were interviewed, prescribers were surveyed and an infectious disease prescriber was consulted to provide prescriber related comments. It was found that meropenem use can be optimised in several areas including; appropriate dosing, use of sensitivity data, infection control and prevention and stock management. A few of the critical interventions recommended to address these problems include; the updating of the *Indications for Meropenem use at Divisional Hospitals Policy*, development of the *Meropenem Treatment Guideline*, microbiology results be made available on PatisPlus®, development of stock management standard operating procedures and all cases of multi-resistant organisms to be treated as an outbreak. A strategic plan is recommended to be developed by each CWMH department involved which will include how to successfully implement and monitor the recommended interventions to reduce inappropriate meropenem usage and prevent development of antibiotic resistance.

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Appendix 1. Indications for Meropenem Use at Divisional Hospitals Policy

Policy

National Medicines & Therapeutic Committee

Indications for Meropenem Use at Divisional Hospitals Policy



INDICATIONS FOR MEROPENEM USE AT DIVISIONAL HOSPITALS POLICY

Revised version of, Endorsed Amendment on the 4th National Medicines & Therapeutics Committee meeting, 20th June 2008

Meropenem is a broad-spectrum antibacterial agent, with activity against the majority of Gram positive, Gram negative and anaerobic bacteria. As such, its use and misuse raises the potential for the development of significant bacterial resistance with profound clinical impact. Meropenem is also very expensive. For these two reasons, its use at the three divisional hospitals (CWM, Lautoka and Labasa) must be very strictly limited.

Meropenem may be provided for the following clinical indications:

1. In any individual patient where there is clear clinical evidence of infection

PLUS

A blood culture plus other relevant body fluids confirmed positive for an organism shown to be resistant to all other available (or appropriate) antibiotics.

2. During a confirmed outbreak of an organism resistant to all other available (or appropriate) antibiotics in the Intensive Care Units only (NICU, PICU or adult ICU), as **empirical therapy for patients with clinical evidence of infection, for a maximum of 72 hours pending results of microbiology specimens. If infection with a multi-resistant organism is not microbiologically confirmed at this time, meropenem must be ceased and appropriate alternative antimicrobial therapy instituted.** Once the outbreak is declared controlled by the Infection Control Unit, empirical antibiotic therapy must revert to a non-meropenem containing regimen.

In both situations the duration of treatment should be the decision of the treating Consultant.

Procedural Requirements¹ – provided the above criteria are satisfied:

1. Treating Unit

Consultant completed *Restricted Antibiotic Form* with attached microbiology results to be submitted to In-patient Pharmacy.

2. Divisional Hospital Pharmacy

Principal Pharmacist to be notified by In-patient Pharmacy, and a *Request for Non Formulary Medicine Purchase* (Form 3, EMF) shall be completed. The *Request for Non Formulary Medicine Purchase*, *Restricted Antibiotic Form* and attached microbiology results are to be faxed to 3388003, attention: Essential Medicines Authority (EMA).

3. Fiji Pharmaceutical and Biomedical Services (FPBS)

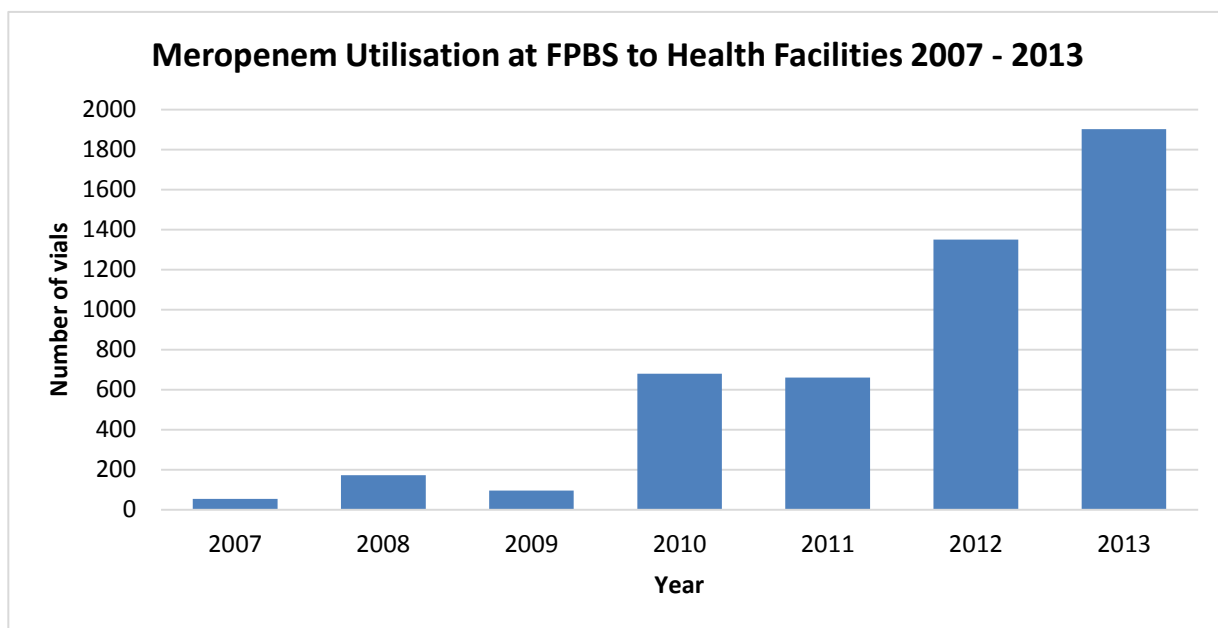
FPBS is to keep a minimum stock of 40 (forty) vials of meropenem 500mg at all times, to be issued promptly on EMA's receipt of the above specified forms. Procurement may reorder stock to a maximum level of 80 (eighty) vials of meropenem 500mg when stock has been depleted to the minimum specified level. EMA to ensure Secretary, National Medicines and Therapeutic Committee is notified of the request. *NOTE: Labasa Hospital Pharmacy authorised to keep six (6) vials on hand at all times for 24 hours use.*

Feedback

It is compulsory for the divisional MTC to present the meropenem case at the next NMTC meeting to brief the Committee on the impact of the use of meropenem.

¹Procedural Requirements revised by Essential Medicines Authority 10th January 2009.

Appendix 2.



Appendix 3. The Restricted Antimicrobial Request Form used at CWMH

CWM Hospital Pharmacy Department

RESTRICTED ANTIMICROBIAL REQUEST FORM

TO BE COMPLETED BY A CONSULTANT

(This form must be completely filled before sending down to the Pharmacy)

Section: A – Patient Details

Patient's Name: _____ NHN: _____

Age: _____ Weight (pediatric only): _____ Ward: _____

Section B – Drug Details

Antimicrobial Requested: _____

Dose: _____ Route: _____ Frequency: _____ Duration: _____

Indication of Use: _____

Specimen for sensitivity test: _____

Date specimen taken & sent to lab
(for follow-up purposes by pharmacist): _____

(This Section Is Not Applicable to *Antifungals and Antiviral*)

Other Antibiotics tried	Duration of therapy
1. _____	_____
2. _____	_____
3. _____	_____
4. _____	_____

Registrar requesting (Name): _____ Signature: _____

Authorized by Consultant (Name): _____ Signature: _____

Date: _____

(Note: Interns Not To Sign The Form)

Justification for Therapy by Prescriber:

Section C -- Antibiotic Sensitivity Report

(To be completed by the Microbiology Dept. in 48 hours before supply continues)

Specimen: _____ Lab No: _____ Date: _____

Organisms: 1. _____
2. _____
3. _____

Technician Name _____ Signature _____

Sensitivity Test	Organism		
Agent	1	2	3
Penicillin			
Amoxycillin			
Erythromycin			
Tetracycline			
Cefaclor			
Chloramphenicol			
Amoxycillin/ Clavulanic Acid			
Gentamycin			
Cephalexin			
Cloxacillin			
Trimethoprim/ SXT			
Nitrofurantoin			
Piperacillin			
Ciprofloxacin			
Ceftioxone			
Vancomycin			
Meropenem			
Amikacin			
Fusidic Acid			

Appendix 4. Data collection Excel® spread sheet

Patient Details				Empirical Antibiotic Requested						Previous Antibiotic Therapy		Empirical Prescribing Approval		Prescriber Justification
Sex	Age	Weight	Ward	Medication	Dose	Route	Frequency	Duration	Indication	Medication	Duration of therapy	Registrar	Consultant	

Specimen Sensitivity						Antibiotic Prescribing		
Specimen	Date specimen taken to lab (Pharmacist follow up)	Date results forwarded to Prescriber & Pharmacy	Within 48 hour window?	Organisms Identified	Sensitive Antibiotics	Antibiotic Therapy Prescribed and Dispensed	Adheres to Sensitivities?	Explanation for prescribing

Appendix 5. Prescriber Survey

Thank you for taking the time to sit with me to answer a few questions and discuss Meropenem prescribing and STGs.

1. Type of Prescriber

- ☐ Medical Officer
- ☐ Resident
- ☐ Registrar
- ☐ Consultant

2. Specialty _____

3. Are you aware of the *Indications for Meropenem Use at Divisional Hospitals Policy*? (Copy shown)

- ☐ Yes
- ☐ No

4. Which one of the following best describes your feelings about and use of the Divisional Hospital's Policy:

- ☐ I refer to the policy frequently, it is an invaluable resource
- ☐ I refer to the policy sometimes, it is an invaluable resource
- ☐ I don't refer to the policy often, but it's reassuring to know it is there
- ☐ I don't refer to the policy at all, but it's reassuring to know it is there
- ☐ I never refer to the policy because I have no need
- ☐ I don't have access to the policy but would like to
- ☐ Other (please specify) _____

5. Are you aware of the *Restricted Antimicrobial Request Form*?

- ☐ Yes
- ☐ No

6. Do you use it every time you prescribe Meropenem?

- ☐ Yes
- ☐ No
- ☐ Only Sometimes, because (please specify) _____

7. Do you have copies of the Fijian Standard Treatment Guidelines?

- ☐ Yes, hard copy
- ☐ Yes, electronic copy
- ☐ No. Why? (please specify) _____

8. Which STGs do you have access to?

- ☐ Antibiotic
- ☐ Cardiovascular
- ☐ Diabetes
- ☐ Emergency
- ☐ Gastrointestinal
- ☐ Psychiatry
- ☐ Respiratory

9. During your clinical practise do you refer to them:

- ☐ Daily
- ☐ Weekly
- ☐ Monthly
- ☐ Less than monthly
- ☐ I'm very familiar with the contents that I don't need to refer to them often

10. Which one of the following best describes your feelings about and use of the Standard Treatment Guidelines:

- ☐ I refer to the Guidelines frequently, they are an invaluable resource
- ☐ I refer to the Guidelines sometimes, they are an invaluable resource
- ☐ I don't refer to the Guidelines often, but it's reassuring to know they are there
- ☐ I don't refer to the Guidelines often, because I am very familiar with the recommendations
- ☐ I don't refer to the Guidelines at all, but it's reassuring to know they are there
- ☐ I never refer to the Guidelines because I have no need
- ☐ I don't have access to the Guidelines but would like to
- ☐ Other (please specify) _____

11. Are there any clinical topics not currently covered in the STGs that you would find useful?

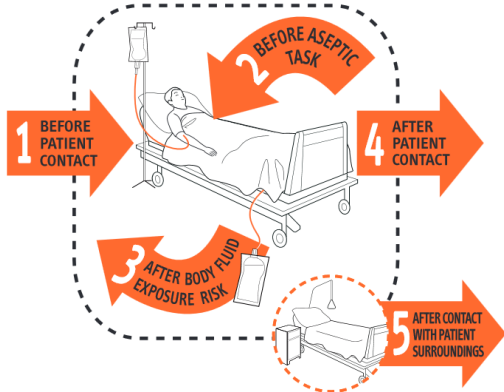
- ☐ No, the STGs cover all clinical topics I need as a prescriber
- ☐ Yes, I would find the following clinical topics useful as they aren't covered in the STGs:

12. What other resources do you refer to for information on the management of STG conditions (eg textbooks, guidelines, websites)? Please specify:

13. Please provide any additional comments, recommendations, or general or specific feedback about the STG topics that we should consider for the next update:

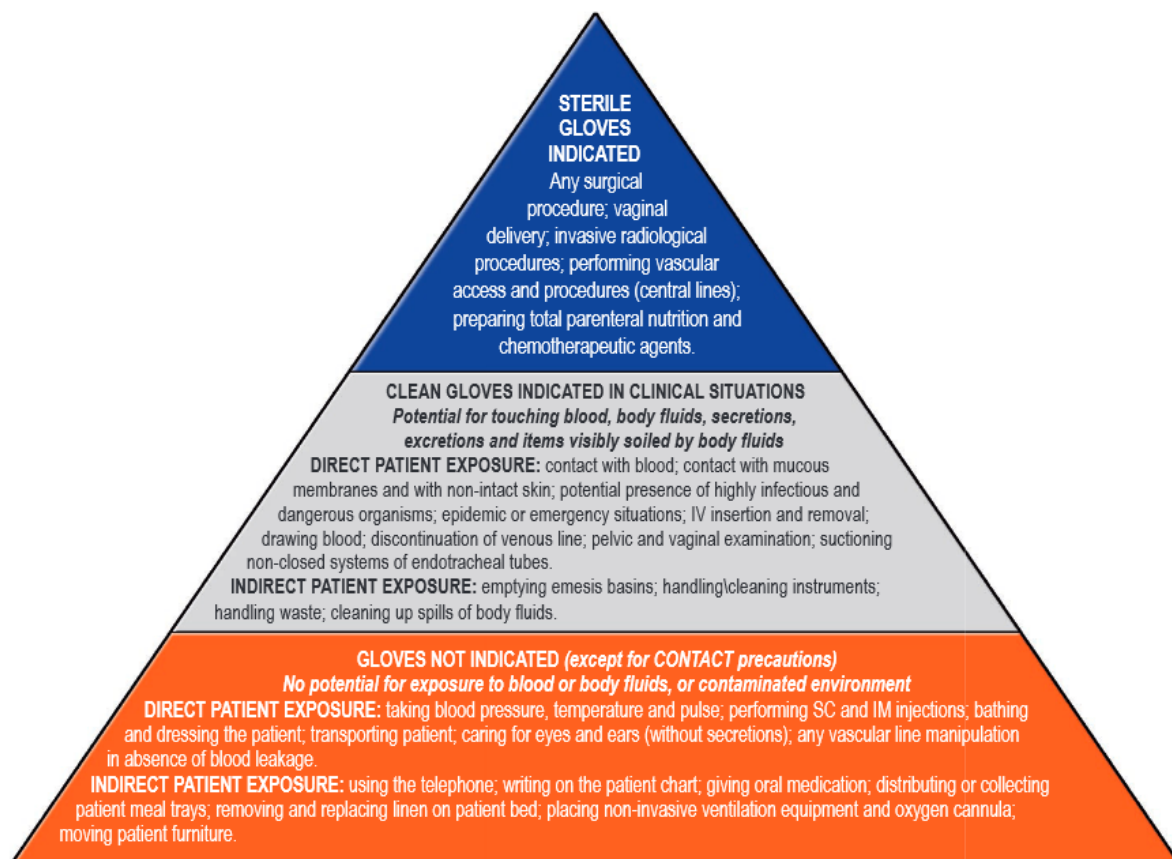
Appendix 6. The WHO Your 5 moments for Hand Hygiene (7)

Your 5 moments for HAND HYGIENE



1 BEFORE PATIENT CONTACT	WHEN? Clean your hands before touching a patient when approaching him or her WHY? To protect the patient against harmful germs carried on your hands
2 BEFORE AN ASEPTIC TASK	WHEN? Clean your hands immediately before any aseptic task WHY? To protect the patient against harmful germs, including the patient's own germs, entering his or her body
3 AFTER BODY FLUID EXPOSURE RISK	WHEN? Clean your hands immediately after an exposure risk to body fluids (and after glove removal) WHY? To protect yourself and the health-care environment from harmful patient germs
4 AFTER PATIENT CONTACT	WHEN? Clean your hands after touching a patient and his or her immediate surroundings when leaving WHY? To protect yourself and the health-care environment from harmful patient germs
5 AFTER CONTACT WITH PATIENT SURROUNDINGS	WHEN? Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving - even without touching the patient WHY? To protect yourself and the health-care environment from harmful patient germs

Appendix 7. Glove use (8)



Gloves must be worn according to STANDARD and CONTACT PRECAUTIONS. The pyramid details some clinical examples in which gloves are not indicated, and others in which clean or sterile gloves are indicated. Hand hygiene should be performed when appropriate regardless of these indications for glove use.