FEEDBACK TO STUDY SITES

ARE NURSE DRUG ADMINISTRATION PRACTICES CONTRIBUTING TO ANTIMICROBIAL RESISTANCE:

CARBAPENEM ADMINISTRATION IN SELECTED PUBLIC AND PRIVATE INTENSIVE CARE UNITS IN KWAZULU-NATAL, SOUTH AFRICA

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REPORT TO STUDY SITES

Please note that this is an abbreviated report. The complete thesis and articles are available on request. I would like to express my sincere gratitude to all hospitals who supported this research. In particular, I would like to thank the nursing staff who welcomed me into the ICUs for the long periods of research. I trust the feedback within this report will be useful.

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ABBREVIATIONS

Antimicrobial Research Unit (ARU) UKZN,

Antimicrobial resistance (AMR)

Antimicrobial stewardship (AMS)

Biomedical Research Ethics Committee (BREC

Carbapenemase-producing Klebsiella pneumoniae (CPKP)

Carbapenem-resistant Enterobacterales (CRE)

Clinical facilitator (CF)

Endotracheal aspirates (ETA)

Enrolled nurse (EN)

Infection prevention and control (IPC)

Intensive care units (ICUs)

Intravenous (iv)

Knowledge, attitudes and practices (KAP)

KwaZulu-Natal (KZN)

Length of stay (LOS)

Medication administration errors (MAEs)

Minimum inhibitory concentration (MIC)

Multi-drug-resistant organisms (MDROs)

National Health Laboratory Services (NHLS)

National Institute for Communicable Diseases in South Africa (NICD)

Registered nurse (RN)

Standard Operating Procedures (SOP)

Whole genome sequencing (WGS)

ABSTRACT

Background: The nurses' role in the multidisciplinary antimicrobial stewardship (AMS) team focuses on infection prevention and control (IPC) and antimicrobial drug administration but may not have explored all gaps within nurse practice in terms of the latter. This study examines an aspect of clinical nurse practice that may be unknowingly exacerbating antimicrobial resistance (AMR). Nurses may be contributing to AMR by sub-optimal administration of intravenous (iv) antimicrobial infusions that may fail to deliver the correct dosage regimen.

Aim: To ascertain whether nurse iv administration practices of carbapenems have the potential to result in infection or colonization with carbapenem-resistant Enterobacterales (CRE) in selected public and private general intensive care units (ICUs) in KwaZulu-Natal.

Methods: This observational exploratory study assesses the administration process of intermittent carbapenem infusions and implications for patient recovery/deterioration, within three general ICUs in KwaZulu-Natal. It was undertaken in three stages;

Stage One: Describing AMS guidance to hospital-based nurses;

Stage Two: Analysis of ICU nurse knowledge, attitudes and practices of iv antibiotic administration in relation to AMR and AMS

Stage Three: Examining ICU nurse carbapenem infusion administration practices.

Results: *Stage One,* scoping review of key AMS guidelines (n=43) revealed minimal inclusion of and guidance to bedside nurses, highlighting a slow but incremental increase in recognition of their role. In *Stage Two*, the questionnaire-based survey amongst ICU nurses yielded a response rate of 42.9% and showed inadequate knowledge, attitudes and practices, with insufficient access to AMS and antibiotic best practice guidance within all study sites. *Stage Three* entailed enrollment of 105 patients, 20 of whom were observed during carbapenem administrations (n=223 observations). Multiple process errors were found at both preparation and administration phases in all administrations. Medication safety measures (double-checking and infusion bag labelling (91.7%)) were not adhered to. There was incorrect 'signing off' of dose administration time on medication chart (72.6%). Poor adherence to scheduled time of administration resulted in incorrect

dosing intervals (65%). There was non-compliance with prescribed infusion duration (40%). There were incorrect number of vials reconstituted (1.4%), and missed doses (5.4%). Reconstitution of vials used varying volumes of diluent, many inadequate (53.4%). Volumetric analysis of discarded equipment found mean loss of the antibiotic dose in: vials (4.9%), syringes (1.2%), infusion bags (6.3%), and infusion lines (30.8%), and subsequent non-delivery of the full prescribed dose (100%). Six patients were colonized with CRE (n=20, 30.0%). Microbial culture and susceptibility analysis of blood and other cultures (endotracheal aspirate (ETA), urine, and wound specimens) showed carbapenem resistance in seven patients (n=20, 35.0%) and multidrug resistance in eight patients (n=20, 40.0%).

Conclusion: The lack of active AMS in the study ICUs seen both pre- and during the Covid-19 pandemic, suggests that this initiative needs support at hospital management level, and most certainly, impacted on nurse understanding of AMS and AMR. It is recognised that multifactorial risks for resistance include admission to an ICU, debilitation accompanying critical illness, presence of invasive devices, inappropriate prescribing of antimicrobial medicines, and horizontal transmission. However, attention must also be focused on the optimal administration of antimicrobial infusions and should be considered in creating strategies for the prevention of AMR.

Keywords

Antimicrobial stewardship; Carbapenems; Dose optimization; Drug resistance; Intensive care units; Medication errors; Patient safety

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

- AMR is a challenge to the care of critically ill patients.
- Nursing students are not exposed to the same level of AMS education as other healthcare disciplines.
- Hospital AMS teams do not include nurses in discussions and decision-making.
- Nursing AMS responsibilities are highlighted as: monitoring and communicating clinical trends to clinicians; culture taking and communication of results to clinicians; administration of antimicrobial medicines; monitoring duration of treatment and de-escalation of antimicrobial medicines; and comprehensive IPC measures.
- Medication administration errors (MAEs) pose a challenge in healthcare setting, particularly in acute care areas.
- Risk mitigation measures include double-checking of medications, especially parenteral medications.
- There is a lack of clarity regarding flushing of administration lines following intermittent medication infusions.

CONTRIBUTIONS OF THIS STUDY TO AMS LITERATURE

1) The study identifies a persisting lack of antimicrobial stewardship guidance to bedside nurses.

- The structured review of key AMS guidelines showed the relatively recent identification of the bedside nurse AMS role and responsibilities and may be lagging behind nursing and other multi-disciplinary healthcare discussion/recommendations.
- The structured review of AMS literature highlighted recommendations within key international AMS guidelines for the education of bedside nurses in their AMS role within formal, informal, and clinical-based education.
- Contributions of ICU Nursing Managers and nurses in the study ICUs, within the knowledge, attitudes, and practices questionnaires, indicated a lack of AMS activity and guidance.

2) MAEs involving antimicrobial medications should be considered as high-risk errors, with the potential to contribute towards AMR.

- Double-checking of the prescription and antimicrobial medication was sub-optimal, thus negating risk mitigation measures.
- The time of administration of the medication did not always coincide with scheduled times and was incorrectly signed off on medication charts as given at the scheduled time, adversely impacting required antimicrobial timing intervals, and potentially compromising multi-disciplinary communication.
- Labels containing details of the patient receiving the medication, medication and dose, and date and time, were either not placed on the infusion bags, or incomplete, increasing the risk of miscommunication within the ICU team.
- Antimicrobial treatment was not always administered at the prescribed dosing intervals, thus impacting minimum inhibitory concentrations (MIC).
- Antimicrobial infusions were not always administered over the desired duration of time, thus impacting MIC. This has implications in the correct use of time-dependent broad-spectrum antibiotics such as carbapenems.
- Data from this clinical study adds important information to current theoretical discussion in the literature around small volume bag intermittent infusions and the implications of a dearth of flushing guidance to clear the infusion administration line of residual drug.

- Data also demonstrates that there is loss of medication dose to all discarded infusion items (vial, syringe, bag, line), raising general concerns regarding loss of dose in other types of intermittent medication infusions.

3) Varying practice in administration of intermittent antimicrobial infusions is a potential contribution to AMR.

- This study also demonstrates that although the small numbers of patients studied may pose difficulty in formulating statistical associations, the theoretical associations between administration practices and AMR could be made.
- This study, therefore, places a spotlight on basic nursing practice. Medication administration constitutes a large part of daily work, and pre-registration education correctly enforces the 'rights of medication administration'. Medication errors involving antimicrobial medications should therefore be considered in the provision of AMS and should be monitored by the AMS team in the clinical environment.

4) Prescribing practices

- The prescription of carbapenem treatment to patients within public ICUs is less than in the private sector, possibly due to formulary restrictions (cost containing measures and AMS).
- It was not common practice within the private ICU to take cultures to guide antimicrobial treatment.

5) Transmission concerns

- Open plan ICUs create conditions in which resistant pathogens may be transferred between patients.
- Inadequate IPC creates conditions in which resistant pathogens may be transferred between patients.

EXECUTIVE SUMMARY OF STUDY RESULTS

- Examination of nursing iv guidelines shows detailed instructions for flushing after iv injection but not for flushing administration lines following administration of an intermittent medication infusion.
- Current literature suggests that administration of intermittent antimicrobial infusions may not be delivering the complete intended dose and that this is particularly due to a lack of direction or uncertainty in regard to correct flushing practices.
- In view of little research considering this issue, we worked from the premise that priming volume was equal to the amount of volume that was not delivered, if not flushed.
- We used literature alerting that undelivered residual volume containing medication was of concern: *Nursing literature*;[1-11] *Pharmacist literature*;[12-18] *Medical literature*;[19] and *Biomedical Technologists*.[20,21]
- We extended this to define undelivered carbapenem doses as: dose reconstituted but not all withdrawn from the vial, dose remaining in the syringe, dose remaining in the infusion bag, dose remaining in the administration line, and dose remaining in the drip chamber. All these items were retrieved at the bedside while the nurse was in the process of discarding them. Volumetric analysis was not conducted on items that were not retrieved.
- We based our practice expectations on prescribed doses. The study did not interrogate prescriber decisions on the antibiotic, dose, division of doses over 24 hrs etc. Our study was observing infusion practice in its entirety. So, did the right patient receive the right antibiotic, was it reconstituted correctly, was the full dose inserted into the saline infusion bag, was it given at the correct time, was it given over the correct duration, was the full dose given, was this correctly documented, and so on.
- We worked on the theoretical assumption that the carbapenem prescribed was chosen in response to the patients' clinical condition, that is, infection markers, microbiology cultures etc. And that the dose was chosen appropriately to meet MIC for that pathogen.
- We attempted to monitor resistance in our study patients by tracking changes in gut commensals. Serial rectal screening of all patients receiving carbapenem infusions (including: ertapenem, imipenem, doripenem and meropenem) was undertaken to document any incidence of CRE colonisation/infection. This has serious repercussions for patients with a mortality rate

of over 40%,[22] and even if colonised this is problematic.[23] CRE is highly transmissible, with implications for healthcare staff, other patients, the hospital environments, and the patients' communities on return home.

- We also monitored cultures of blood, endotracheal aspirates (ETA), urine, and wounds, as our study patients developed multi-drug-resistant pathogens (apart from carbapenem resistance). Finally, we monitored days spent in ICU, length of stay (LOS) (which allows us to understand the severity of the patient's illness), and death.
- We then extended the information gained from the CRE isolates, with a further study conducted by a post graduate student in the Antimicrobial Research Unit (ARU) UKZN, with whole genome sequencing (WGS) by the National Institute for Communicable Diseases in South Africa (NICD). This indicated that a new sub-strain of *K. pneumonia* was emerging in this area of South Africa.[24]
- Additionally, participation (JR) on an international panel on undergraduate nurse AMS competences,[25] confirmed that the practical aspects of antimicrobial infusion administration were not a considered issue when formulating these competencies.

CHAPTER ONE: INTRODUCTION TO THE STUDY

1.1 Background to the study

The selective pressure that results from exposure to antibiotics highly correlates with the emergence of resistance.[26,27] In this study, I argued that clinical roles of the nurse preventing and containing AMR should be considered (Rout et al., 2019). For the past two decades, AMS has placed a focus on addressing prescribing behaviour. Additionally, there has been a concerted effort by healthcare societies and institutions to advocate for and improve IPC measures in clinical environments. Hospital-based IPC protocols for addressing potential root causes of the spread of antimicrobial-resistant infections have become formalized in healthcare facilities and primarily focused on improving nursing practice,[28-31] but little attention has been placed on other nurse practices that might contribute to AMR such as medication administration practice.[32-35] The nurses' role in the multidisciplinary AMS team thus focuses on IPC and monitoring antimicrobial drug prescription but may not have explored all gaps within nurse practice in terms of ensuring optimal antimicrobial treatment.

This study therefore does not question the appropriateness of the choice of drug for the diagnosed infection, but considers what potentially might happen should the drug not be given as prescribed. The optimal administration of intermittent antimicrobial infusions intends to arrest the disease process, achieve the desired treatment of infection, prevent complications such as AMR, and return to health. It is therefore important that intended antimicrobial treatment reaches the patient. I contend that nurse knowledge about antimicrobial medicines is limited, impacting on practical administration of antimicrobial medicines and potentially contributing to.[36,37] The premise of this is that current nurse administration of antibiotic infusions may result in non-delivery of the full prescribed dose, resulting in treatment failure, and may unknowingly contribute to AMR within patients receiving this treatment. Sub-optimal infusion nursing practice results in interruption of intended treatment. This could potentially result in the development of resistance in the causative bacteria infecting the patient, with the risk of spreading to the hospital environment and the community. Understanding the drivers of AMR is essential to meet the challenges facing healthcare in the 21st Century.[38] This must include interrogating practices of healthcare professionals.

1.2 Study hypothesis

Intravenous carbapenem administration practices of nurses are flawed resulting in non-delivery of therapeutic dose. This could result in antimicrobial resistance due to antibiotic under-dosing.

1.3 Aim of the study

Sub-therapeutic dosing may contribute to selective pressure that favours the development of antibiotic-resistant organisms,[36,37] therefore, the aim of the study was to ascertain whether carbapenem infusion practices have the potential to exacerbate infection or colonization with CRE within the cohort of patients receiving this treatment.

1.4 Research questions

The research questions addressed during the course of the study were: 'What education and training recommendations do AMS guidelines give regarding intravenous antimicrobial medicines administration practices by nurses?' and 'Are nurses contributing to microbial resistance through antibiotic infusion administration practices that result in inaccurate dosing?'

1.5 Research objectives

Objective 1: To describe and critically examine key global AMS guidelines compiled by national healthcare organisations, interested healthcare societies, and medical and nursing professional bodies.

- To describe the development of the nursing role in AMS within key AMS guidelines.
- To describe specific references to the role and responsibilities of the hospital-based nurse within key AMS guidelines.
- To describe AMS guidance regarding hospital-nurse iv administration of antimicrobial medicines.

Objective 2: To examine and describe nursing knowledge and attitudes regarding iv administration of antimicrobial medicines, within the context of AMS protocols and training available to nurses working in general ICUs.

- To describe ICU/hospital AMS policies and protocols available to nurses working in general ICUs.

- To describe AMS training available to nurses working in general ICUs.
- To describe guidance for nurse intermittent iv administration of antimicrobial medicines within ICU/hospital AMS policies and protocols and the AMS training available to nurses working in general ICUs.

Objective 3: To observe, describe and analyse the preparation and administration phases of carbapenem infusions in general ICUs, in relation to dosing accuracy.

- To measure undelivered carbapenem volume in used vials and iv equipment.
- To track changes in gut commensals by sequential rectal swab sampling for CRE using Chrom-ID selective media at admission to the ICU, at 48 hours, 72 hours, weekly, and on discharge from the ICU/death.

Objective 4: To observe, describe and analyse preparation and administration phases of carbapenem infusions in general ICUs, with a view to the development of recommendations for the improvement of clinical practice.

- To describe different methods of intermittent antimicrobial infusion administration.
- To identify nursing learning needs for additional training in intermittent antimicrobial infusion administration.
- To identify which administration methods of intermittent antimicrobial infusions should be eradicated from clinical nurse practice.
- To make recommendations for nursing education, nursing policy, and nursing clinical practice.

1.6 Conceptual framework

The Leavell and Clark's Levels of Prevention Model (1953)[39] suggests that any disease or injury occurs on a continuum between health and advanced disease. Optimal administration of intermittent antimicrobial infusions can be placed at the second level of Leavell and Clark's model as the appropriate intervention to arrest the disease process, achieve the desired resolution of infection, prevent complications such as AMR, and return to health, and has been used as the model to guide this study.

1.7 Study design

This was an exploratory observational study examining the process of preparation and administration of intermittent carbapenem infusions to critically ill patients within general ICUs. A positivist approach was adopted with quantitative techniques in all three stages of the study: i) structured literature review; ii) analysis of ICU nurse knowledge, attitude, and practice; and iii) observation of nurse administration of intermittent intravenous carbapenem treatment and analysis of rectal swabs to describe changes in patient gut commensals. Although the study was not powered for sample size there was value in that there was more than one set of data. Stage Two and Stage Three are presented in this report to the study hospitals.

1.8 Study sites

Selected hospitals were a regional public hospital, a tertiary public hospital, and a private hospital in KwaZulu-Natal (KZN).

1.9 Ethical considerations

Following institutional ethical approval from the University's Biomedical Research Ethics Committee (BREC BE709/18), the Department of Health Provincial Research Ethics Committee (NHRD (KZ 201905032) and the private hospital group research and ethics board; permission to conduct the study was obtained from hospital and unit management in both public and private hospitals.

1.9.1 Nurse researcher advocacy

Following an application to BREC for amendments to the study protocol, approval was granted to request associated laboratory results with a BREC recommendation for researchers to reduce opportunities for transmission. The importance of maintaining an objective researcher position was very clear to me, but my responsibility as a patient advocate (I felt strongly that I had a nursing responsibility to my study patients) was a daily concern. Following initial meetings with Nursing Unit Managers to further explain the study, it was agreed that I would meet with respective unit managers frequently. This was helpful in facilitating the study. I tried to manage these ethical contradictions by meeting with the Nursing Unit Managers initially and discussing data collection,

then reporting adverse events. This was as discrete as I could make it, aware that nurses delivering care to the study patients might view me as an ‘impimpi’ (informer).

1.9.2 Hawthorne effect

In my view, there did not appear to be a Hawthorne effect to my presence. This was possibly due to my presence every day in the ICUs, and any initial curiosity regarding my presence soon abated as I became just another worker in the unit. Despite my presence, I did not observe improvements in infusion practice during the time spent in each unit.

1.9.3 Undesired dosing

My experience in auditing medication treatment charts meant that I was familiar with desired medication documentation; both that of prescriber, and nurse documentation. However, this form of auditing did not observe medication administration practice. Therefore, if a dose was signed off as given at a particular time, there was no way of checking that this was correct. I became aware early in the study that there was undesired infusion practice: in particular missed doses, incorrect number of vials reconstituted, incorrect timing, and obvious amounts of antibiotic discarded in infusion bags. It was disappointing to observe the extent to which infusion errors occurred, both in documentation and in administration of the drug. This was not anticipated when formulating the study hypothesis, aims and objectives, where I was focused mainly on residual volume within administration lines. This posed an ethical dilemma for me as a registered nurse (RN), which I attempted to resolve by frequent feedback to the Nursing Unit Managers/clinicians.

1.9.4 Transmission

Additionally, although this wasn’t the focus of my study, it was very difficult for me not to be concerned about serious issues in IPC practice with patients with CRE being nursed in open ICU spaces, especially in ICU A where there were no isolation cubicles. Nursing staff used drawn curtains to try and control access to the bedspace of a patient with CRE. However, this was unsuccessful, with physiotherapists, cleaning staff, etc moving freely through the bedspace. This was discussed with the IPC Nursing Manager. ICU C had patients with CRE being nursed in the open unit, despite having some isolation cubicles. These were reserved for post-operative cardiac surgery patients, paediatric patients, and patients who were receiving dialysis. On several

occasions, nurses were allocated to the care of two patients, one being CRE positive. This was a very uncomfortable situation for me, especially as on two occasions the non CRE patients (paediatric, post cardiac surgery) were particularly vulnerable and were being nursed in isolation cubicles because of that concern. Other IPC contraventions in ICU C that concerned me were: uncontrolled movement of non-nursing personnel through the open section of the unit (which had several CRE positive patients); dirty linen placed on the floor; frequent lack of soap and paper towels at hand basins; and nursing staff frequently gathering in an isolation cubicle containing a patient with CRE. This was discussed with the IPC nursing sister, the Deputy Nursing Manager, and the Hospital Manager. Following this meeting, I was concerned about a toddler visiting his mother, a patient in the open section of ICU C, with several known CRE patients within this section. COVID-19 protocols restricted visiting during this time. Rectal swab testing was positive for CRE for this particular patient the following day.

1.9.5 Sampling issues

Although there was a CRE testing protocol within the private hospital, there were no CRE testing protocols in the public hospitals and clinicians welcomed this additional information. Unfortunately, there were logistical problems throughout data collection, even prior to the COVID-19 pandemic, where delays in obtaining testing reagents meant that, on some occasions, identification of CRE came too late to be of clinical value within the ICU. Initial difficulties in accessing Labtrak (the NHLS database) had a similar result. Additionally, there were several submitted swabs which could not be found on Labtrak and were lost to the study, and several results which reported 'lab error'. There were also several anomalies where patients who had previously been identified as CRE, then, on having a subsequent swab tested as CRE negative. This was viewed as 'lab error'. Interestingly, patient C12 tested as CRE negative following two weeks of testing CRE positive. Testing continued and remained CRE negative until the patient's demise six weeks later. This resulted in some confusion in the ICU C as nursing staff were unsure whether to keep the patient in isolation. Unfortunately, the hospital CRE protocol did not support retesting at that stage, so these results were not confirmed by another laboratory.

1.9.6 Interactions with ICU nurses

Although all nurses in each ICU had been given an information letter detailing the research, little interest was expressed in my presence at a study patient's bedside during carbapenem infusions. Nurses appeared more interested in the serial collection of rectal swabs, and in particular sought reassurance that I would not disturb the patient while obtaining the specimen. Shift leaders were informed about positive CRE results. Communication with shift leaders in both the public ICUs was facilitated by their familiarity with research studies in their units and by all shift leaders being ICU trained. This was more difficult in the private ICU where few nurses were ICU trained, and shift leaders were frequently also assigned to primary patients care, often managing two patients in addition to their shift leader responsibilities. These were often focused on obtaining nursing coverage for the following/next day shift.

1.9.7 Interaction with doctors

All doctors were informed of the research. Communication with doctors was generally positive and I was invited to join rounds in the public ICUs. Study patients in the private ICU were managed by various doctors, most of whom were specialists. There was one occasion where I asked a question regarding further courses of meropenem for patient C12 who had tested positive for CRE following the 1st course (also carbapenemases in blood culture), and the doctor informed me that colonisation did not mean infection. The patient received four courses of meropenem before demise.

1.9.8 Interaction with pharmacists

I did not meet any pharmacists during my time in the study ICUs. The hospital manager in the private hospital suggested that I explain the study to the pharmacists, but they were unable to meet with me during the three months that I was daily at the hospital.

1.9.9 Interaction with microbiologists

Although I was informed that the microbiologist accompanied the doctors in the public ICUs on a weekly round, this did not seem to happen. I did, however, get an opportunity to meet a microbiologist in ICU B on one occasion. I did not meet any microbiologists from the private laboratories during my time in ICU C.

1.10 Further analyses of CRE isolates

In a separate study co-supervised by myself (in the capacity of an Honorary Research Fellow affiliated to the Antimicrobial Research Unit (ARU), in the School of Health Sciences (UKZN)), rectal swabs from ICU A (public) with CRE isolates were analysed for antibiotic susceptibility. Isolates positive for carbapenemase-producing Klebsiella pneumoniae (CPKP) were resistant to ertapenem and meropenem (100%), and imipenem (71.4%). Whole genome sequencing (WGS) for CPKP was then carried out by the National Institute for Communicable Diseases (NICD). These sequenced isolates had the blaOXA-181 carbapenemase. They were the same sequence type ST307, and were subsequently entered into the national database as the first incidence of this CPKP strain in KZN. 'All the isolates carried the same virulence repertoire, reflecting the epidemiological relationship between isolates. blaOXA-181 was located on a multi-replicon plasmid similar to that of E. coli p010_B-OXA181, and isolates were aligned with several South African and international clades, demonstrating horizontal and vertical transboundary distribution. The findings suggest that blaOXA-181 producing K. pneumoniae is endemic in this ICU, colonizing the patients'.[24,40,41] These findings supported the installation of isolation cubicles to improve infection prevention and control (IPC) measures[24] in this unit and were discussed with Nursing Management.

1.11 Rout publications relevant to this chapter

Please refer to papers listed below if interested

PRIOR RESEARCH ON THE ROLE OF THE ICU NURSE IN AMS

Rout J, Brysiewicz P. Exploring the role of the ICU nurse in the antimicrobial stewardship team at a private hospital in KwaZulu-Natal, South Africa. *South African J Crit Care* 2017; 33(2):46-50. https://dx.doi.org/10.7196/SAJCC.2017.v33i2.331

Rout J, Brysiewicz P. Perceived barriers to the development of the antimicrobial stewardship role of the nurse in intensive care: Views of healthcare professionals. *Southern African Journal of Critical Care* 2020; 36(1):51-56. http://dx.doi.org/10.7196/sajcc.2020.v36i1.410

CRE COLONIZATION IN STUDY ICU

Madni O, Amoako D, Abia A, **Rout J,** Essack S. Genomic investigation of carbapenem-resistant klebsiella pneumonia colonization in an Intensive Care Unit in South Africa. *Genes* 2021a; 12(7):951. https://doi.org/10.3390/genes12070951

Madni O, Amoako D, Abia A, **Rout J**, Essack S. Colonization in an Intensive Care Unit in the uMgungundlovu District, South Africa. ePoster sessions. European Congress of Clinical Microbiology & Infectious Diseases. 2021b. ECCMID 2021: ePoster Sessions (accessed June, 2022).

CHAPTER TWO: KNOWLEDGE, ATTITUDES AND PRACTICES

2.1 Questionnaire development

In the absence of an existing questionnaire seeking to explore the issues necessary for my research, a questionnaire was designed and developed by myself, and was completed and reviewed for validity and reliability by an expert group of ICU-trained nurses. Following this review, the questionnaire was then reassessed, redesigned and several questions clarified. New questions included: i) Standard Operating Procedures (SOP); and ii) further information on respondent completion of the questionnaire.

2.2 Study Design

This study aimed to describe ICU nurse knowledge, attitudes and practices (KAP) regarding iv antimicrobial treatment and AMS pre-registration training received, access to relevant nursing policies and protocols, and availability of related in-service teaching. Self-administered questionnaires were distributed to bedside nurses in three general ICUs. Nursing Unit Managers were requested to complete two short questionnaires documenting unit demographics and AMS activity in the units: namely any AMS programme/activity, nurse inclusion on the AMS team, frequency of AMS rounds, availability of AMS policies, protocols or guidelines, and training on the administration of intravenous iv antimicrobial medicines.

2.3 Ethical considerations

All nurses working in the study ICUs were invited to take part in the study, were informed of its purpose, and had the right to withdraw at any stage. Written consent was obtained, and anonymity and confidentiality were maintained.

2.4 Sample/Participants

Convenience sampling was conducted of all bedside nurses (allocated to direct patient care) and three Nursing Unit Managers working in the general ICUs of three urban hospitals (one private and two public) in one Health District in South Africa. See Table 2.1 for inclusion/exclusion criteria. However, data collection was disrupted by the Covid-19 pandemic and a year passed before access was again permitted.

2.5 Data collection

ICU Nursing Managers notified nurses about the study and facilitated distribution of the questionnaire to nurses on each shift. The nurses received a package containing an information sheet and a consent form, and were invited to complete an enclosed two-page questionnaire including 4 demographic questions and 25 questions. These were knowledge (12), attitudes (6), and practices (7), intending to cover formal and informal training on administration of iv antimicrobial medicines and AMS. Nurses were requested to post the completed questionnaire and consent form in two separate envelopes in a sealed collection box. The investigator (JR) was present daily to answer questions about the study and to collect completed questionnaires from the collection box.

2.6 Data analysis

Collected data from each study site was tabulated on a spreadsheet (Microsoft Excel for Windows 10), and a statistical analysis using Stata v17 was conducted, with the assistance of a statistician. Descriptive statistics (frequencies and percentages) were used to summarise the research results. Results were stratified by hospital (private versus public), nurse qualifications (enrolled versus registered), years of nursing experience, and whether or not advanced training had been received for example; ICU training. Responses were compared using Fisher's Exact test. Statistical significance was taken at a threshold of ≤ 0.05.

2.7 Results

2.7.1 Response rate

Of the 161 KAP questionnaires distributed to bedside nurses, 69 (42.9%) were completed (Table 2.2). All Nursing Unit Managers in the three study ICUs completed the ICU demographic and AMS questionnaires.

2.7.2 Demographics

Nurse respondents (n=69) were employed in two public ICUs (n=25, 36.2% and n=28, 40.6%) and one private ICU (n=16, 23.2%). Most respondents (n=42, 60.9%) were between the age groups of 30-39 (n=24, 34.8%) and 40-49 (n=18, 26.1%) and were employed on a full-time basis by the hospitals (n=60, 87.0%). Twenty-five (36.2%) respondents had more than 10 years of nursing

experience. Sixty-three respondents had a registered nurse qualification (91.3%) of which 55 (79.7%) were nursing diplomas and eight (11.6%) were nursing bachelor's degrees. Thirty-seven (53.6%) registered nurses additionally had achieved an ICU diploma. Four (5.8%) respondents (enrolled (EN)) had a two-year nurse certificate. Two respondents did not answer this question.

2.7.3 ICU Nursing Manager questionnaire

All Nursing Unit Managers reported no AMS activity during the Covid-19 pandemic. Prior to that, there was minimal AMS activity in ICU A (i.e., no team or programme), although the Nursing Unit Manager reported that if any teaching occurred, it was given by the doctors. Nursing Unit Managers of both ICU B and C reported AMS programmes prior to the pandemic. Weekly AMS rounds were held in both these units, and the pharmacist was reported to be the person providing the most AMS activities. Only ICU C reported nurses on the AMS team, although AMS rounds and other activities were discontinued during the Covid-19 pandemic. Only this unit was reported to have a written AMS protocol. Nursing Unit Managers reported that none of the units had specific protocols guiding nurse administration of iv antimicrobial medicines, although ICU C's Nursing Unit Manager reported that necessary information was given to nurses on induction to the hospital and then by the clinical facilitator (CF) within the unit.

2.7.4 ICU nurse questionnaire

The survey yielded an ICU nurse response rate of 42.9% and showed inadequate knowledge, attitudes and practices, with insufficient access to AMS guidance within all study sites. Responses from nurses showed that AMS was minimal even before the Covid-19 pandemic, with little access to teaching and guidance (46.4%) within the units, and may have impacted nurse knowledge of AMS principles that aim to prevent AMR. Nurses were not sure that an antibiotic policy existed or where this might be kept in their unit. This combined with only 30.4% of nurses reporting in-service on iv administration of antibiotic medications, is concerning. Non-responses within the questionnaire were the highest (mean 20.9%) to questions testing basic knowledge of antimicrobial groups (Q.4 a-e). Respondents who did answer these questions on antibiotic groups scored poorly (55.7%) (Table 2.3).

2.7.5 Management of intravenous lines

Although nurses administered antimicrobial medicines to patients by all routes, and although it is common practice for patients admitted to an ICU to have some form of intravenous access via either a central line or at least a peripheral line, only 45 respondents (65.2%) reported that they administered iv infusions. An additionally confusing response was that only 89.9% of nurses had used an infusion pump. Thirty-five nurses (50.7%) reported using a dedicated antibiotic line with 31 nurses (44.9%) stating that they used the iv-antibiotic line to deliver intermittent non-antibiotic medication such as iv paracetamol (Perfalgan). Three respondents (4.3%) added a note stating that an intermittent medication infusion such as KCl would not be administered through the antimicrobial medicines dedicated line (Table 2.2).

2.7.6 Flushing practice

Although the study questionnaire did not specifically use the term 'flushing', questions related to flushing practice and may be significant in discarding administration lines that still hold antimicrobial medication. Thirty-nine nurses (56.5%) (public ICU, 62.3%, private ICU, 37.5%) reported that the line was cleared of *other medication* between medication doses (Table 2.4). Respondents (82.6%) reported compliance with local hospital IPC recommendations for infusion administration line changes every 72 hours.

2.8 Rout publications relevant to this chapter

Please refer to papers listed below if interested

NURSE KNOWLEDGE, ATTITUDES AND PRACTICES

Rout J, Essack S, Brysiewicz P. Knowledge, attitudes and practices of administration of intravenous antimicrobial medicines among intensive care nurses: A descriptive cross-sectional study. Accepted for publication. *South African J Crit Care* 2024.

STRUCTURED LITERATURE REVIEW

Rout J, Essack S, Brysiewicz P. Guidelines for the hospital role of the clinical nurse in antimicrobial stewardship: A scoping review. *South African J Crit Care* 2021; 37(2):70-76. https://doi.org/10.7196%2FSAJCC.2021.v37i2.481

Rout J, Essack S, Brysiewicz P. Guideline recommendations for antimicrobial stewardship education for clinical nursing practice in hospitals: A scoping review. *South African J Crit Care* 2021; 37(3):104-114. https://doi.org/10.7196/sajcc.2021.v37i3.482

UNDERGRADUATE AMS EDUCATION

Courtenay M, Castro-Sánchez E, Gallagher R, McEwen J, Bulabula A, Carre Y, Du Toit B, Figueiredo R, Gjerde M, Hamilton N, Jorgoni L, Ness V, Olans R, Padoveze M, **Rout J**, van Gulik N, Van Zyl Y. Development of consensus-based international antimicrobial stewardship competencies for undergraduate nurse education. *J Hosp Infect* 2019; 103(3):244-250. https://doi.org/10.1016/j.jhin.2019.08.001

CHAPTER THREE: OBSERVATION OF CARBAPENEM INFUSIONS

3.1 Study design

This part of the study aimed to observe, describe, and analyse the preparation and administration phases of intermittent carbapenem infusions delivered to study patients. This intended to document the entire infusion process and identify areas of error within the context of possible harm to the patient based on the study hypothesis that intermittent intravenous carbapenem infusion administrations are flawed, resulting in non-delivery of a therapeutic dose.

3.2 Ethical considerations

Patients (or family members in the event that the patient was unable to communicate) consented to the observation of carbapenem infusions and the collection of data. Written informed consent was obtained, and confidentiality was assured after being informed of the purpose of the study and the right to withdraw at any stage. All clinicians and nurses working in the ICUs were informed of the purpose and conduct of the study. I was present daily in the ICUs for extended periods during the hours of 05h00-22h00 to allow opportunities to observe antibiotic administration to study patients prescribed carbapenem antimicrobial medicines. This allowed for any questions or concerns to be addressed.

3.3 Sample/Participants

A convenience sample of patients was accepted with all adult patients admitted to the ICUs being eligible for recruitment (Table 3.1). Enrollment of patients continued for 28 days in each ICU with data collection continuing until these patients left the study, on discharge from the ICU or death. The first study ICU was a regional public hospital; next of kin were often not identified/contactable at admission and meant that intubated patients were not enrolled onto the study. It was important that the admission rectal swab was taken as soon as possible after entry of the patient into the ICU environment to exclude community CRE. The Biomedical Research Ethics Committee (BREC), UKZN, supported a proxy consent from the head intensivist which allowed enrollment of patients onto the study with subsequent consent obtained from the patient/next of kin where possible. There were no occasions where patients/next of kin revoked proxy consent.

3.4 Data collection

Data collection was conducted from March 2020 - July 2021; interrupted by the advent of the COVID-19 pandemic. Medication treatment charts of study patients were inspected twice daily to monitor antimicrobial treatment management. Patients who were prescribed carbapenem treatment were then placed on an observation protocol to monitor the scheduled administration of the medication. Observations were conducted from 05h00 to 22h00 and covered all days of the week in order to observe as many administrations as possible. A new data collection chart was used for each carbapenem administration for each patient and included the date and time, the study ICU number, patient number, and dose number. A structured checklist, developed for the study to strengthen objectivity, allowed data to be collected including the prescribed carbapenem treatment, dose required, scheduled time of dose, observed time that the dose given, the time noted by the nurse on the medication chart, and the duration of the infusion. Infusion bags were inspected for: i) type of nurse labelling; ii) patients name and number; iii) carbapenem name; iv) dose; v) date; vi) time; vii) signature of RN reconstituting and administering the dose; and viii) signature of nurse counter-checking. Serial rectal swabs were taken and analysed (both public and private study patients) by the National Health Laboratory Services (NHLS) to isolate CRE using Chrome-ID selective media. Discarded intravenous administration equipment such as vials, syringes, infusion bags and intravenous administration lines were retrieved where possible, residual volume measured and percentage of drug lost calculated. One researcher (JR) conducted all tests, observed infusion practice, and retrieved used equipment discarded during reconstitution and administration of carbapenem infusions, to ensure reliability and consistency.

3.5 Data analysis

Data were tabulated and statistically analysed. Descriptive statistics were obtained using Microsoft (MS) Excel (for Windows 10). Categorical data from groups were tested for association using Pearson's Chi square, provided that all expected cell frequencies were equal to or greater than 5, otherwise Fisher's Exact test was used. A continuity correction (Yates) was used if the total of all cells was less than 40. Numerical data were described using mean (standard deviation) or median (interquartile range) as appropriate. A p-value of <0.05 was considered statistically significant. Confidence intervals were provided. Groups tested for associations were: i) private hospital ICU and public hospital ICUs; ii) day and night shifts; iii) weekday, and weekend or public holiday

shifts; iv) ICU-trained and non- ICU-trained registered nurses; and v) hospital employed nurses and agency nurses (private ICU only).

3.6 Results

3.6.1 Demographics

Of the 105 patients enrolled in the study, 31 were admitted to ICU A (public regional), 52 to ICU B (public tertiary), and 22 to ICU C (private) (Table 3.1). A subset of patients treated with the carbapenem group of antimicrobial medicines were observed during preparation and administration of this treatment. Twenty-two study patients were prescribed carbapenem antimicrobial medication, with two excluded from analysis in this paper, one due to carbapenem treatment having commenced on transfer from one study ICU to the other and the other due to carbapenem treatment being discontinued on the day of enrollment to the study. Twenty patients (19%) (ICUs A & B: trauma 7, and surgical 4; and ICU C: surgical 2, cardiac surgical 2 and medical 5) collectively received 389 carbapenem doses during their ICU stay, (332 doses during observation periods of 05h00 to 22h00). The researcher was present on 184 shifts for extended periods during which 223 (67.2%) dose administrations were observed:

- 142 meropenem (n=177, 80.2%)
- 63 imipenem (n=124, 50.8%)
- 11 doripenem (n=20, 55.0%)
- 7 ertapenem (n=11, 63.6%)

3.6.2 Medication orders on patient treatment charts

Antibiotic orders included the type of carbapenem, the dose, and the frequency over 24 hours. These orders were later annotated when the clinician wanted the medication stopped. Only one order included the duration of the infusion. No loading doses were ordered on commencement of a course of carbapenem. Twenty-five courses of carbapenems were prescribed; meropenem (48%), imipenem (40%), ertapenem (8%), and doripenem (4%). Seventeen patients received one course, two patients received two courses each of imipenem, one patient received ertapenem followed by a course of meropenem, and one patient received 4 courses of meropenem. Carbapenem prescribing practices appeared constrained within the public ICUs by formulary restrictions (ICU A: 3 out of 31 patients; ICU B: 8 out of 52 patients). This may have been partly due to cost issues

and partly to a Pharmacy AMS drive to control broad-spectrum use. This didn't appear to be the case in the private ICU where carbapenems were used more frequently (ICU C: 9 out of 22 patients).

3.6.3 Rectal swab protocol

Although all study patients had the rectal swab protocol on admission, at 48 hours, 72 hours, weekly, and on discharge from the ICU or death, patients prescribed carbapenem treatment had rectal swabs taken every second day while on carbapenems. This reverted to the original testing regime once carbapenems were stopped. Swabs were processed through the NHLS: facilitated by the head microbiologist at the main laboratory. Neither of the two public ICUs included CRE screening in their admission protocol so the research results were clinically helpful at times.

3.6.4 Medication safety measures

The aim of this part of the study was to observe compliance with prescription instructions for dose timing, and duration. The process of double-checking was observed in the context of medication safety measures. Medication administration practices were observed for double-checking of the medication order, medication vial, and method of preparation and administration. Infusion administrations (n=223) were observed on 20 patients prescribed carbapenem treatment. Patient medication treatment charts were inspected for nurse signature and time written of dose given. One hundred and forty-four infusion bags (64.6%) were retrieved and inspected for labelling information (medication and patient details) at bag changes during the periods of observation (Table 3.2). Although each of the study ICUs had different expectations regarding labelling of intermittent medication infusion bags, it was clear that expectations frequently were not met and medication errors occurred, in particular, errors of omission and timing which were not detected and thus not addressed.

Statistical significance was, however, found in only three areas within the comparison groups. Firstly, *labelling errors* between public (100%) and private (84.6%) units ($p < 0.001$). The supply of pre-printed sticky labels in the private healthcare hospital facilitated the documentation of patient and medication details on the affixed labels. Secondly, *timing errors* seen between agency supplied nurses (78.8%) and hospital employed nurses (58.2%) (p 0.034) (private ICU only).

Timing errors were also associated with day/night shifts; night shift being significantly associated with early administration (39.5%) compared to day shift (22.5%) (p 0.01), and day shift significantly associated with late administration (38%) compared to night shift (18.5%) (p 0.02). And lastly, *dose interval errors* between agency supplied nurses (78.8%) and hospital-employed nurses (58.2%) (p 0.034) (private ICU only). Errors associated with agency supplied nurses could be attributed to the pressures experienced by agency nurses in an unfamiliar environment; however, this is unknown in the context of this study.

3.6.4.1 Double-checking process

Low compliance with double-checking (an important safety component of preventive nurse practice) is of major concern, particularly in the ICU. When double-checking did occur, it was evident that this was variable, resulting in multiple errors: incorrect dose reconstituted and given; missed doses; doses not given at the scheduled time; and/or the actual time of administration either not recorded or misrecorded. Additionally, ENs, who should not have been involved in the process,[42] signed off that they counter-checked a dose. This appeared to be common practice within this one ICU and did not arouse comment. None of the missed carbapenem doses noted during observation periods were identified as missed doses by the ICU shift leaders, possibly due to the bedside nurse signing that the dose had been given at the scheduled time. Medication was prepared at the patients' bedside. Supplies were obtained from a central store area in the public ICU, whereas supplies were kept at each patients' bedside in the private ICU. Nurses were observed carrying the additive medication label away from the patient's bedside to other nurses; requesting a second signature. The drug (vial) and medication chart (prescription) were thus not checked by the checking nurses before signing the label, and checking nurses frequently did not approach the patient's bed space to confirm the identity of the patient.

The names and designations of the nurses mixing and administering antibiotic and the checking nurses were often missing or illegible. Of the 144 infusion bags inspected, 76 (52.8%) infusion bags were unsigned by the primary nurse mixing and administering the dose, making it difficult to confirm whether the dose was given by an RN. Nine ENs (6.3%) signed that they were the primary nurse reconstituting and administering the dose. Counter-checking was signed off in 51 (35.4%) infusions, however, ten (19.6%) signed counter-checks were on labels that did not contain the

primary nurse's signature. Twenty-three (45.0%) counter-checks were signed by RNs and ten (19.6%) by ENs, one of whom was an EN counter-checking another EN mixing and administering the carbapenem infusion (Enrolled nurses have attained a two-year certificate in nursing but may not take primary care of patients in specialised units).[42]

3.6.4.2 Timing of dose

Although initial analysis of data expected administration time at the exact scheduled time, many administrations were a few minutes before or after the hour. This was often due to concomitant patient care. A decision was made to accept the theoretical injunction to administer antimicrobial therapy *as close as possible to* dosing time. An administration period covering 30 minutes around the scheduled dose time (accepted leeway of 15 minutes early/late) was therefore accepted as complying with the administration time. Compliance with dose timing, according to this accommodation, was found in only 78 administrations (35.0%), with an additional twelve (5.4%) doses missed, but charted as administered (Table 3.3). Of 223 carbapenem doses, 145 (65%) were not given as scheduled: 64 (28.7%) given early, and 69 (30.9%) given late. This resulted in incorrect spacing between carbapenem doses. Incorrect dose timing was evident with "6 hourly" doses (imipenem) ranging from 3h50m to 7h30m, "8 hourly" doses (doripenem and meropenem) ranging from 5h to 12h10m, and "daily 24 hourly" doses (ertapenem) ranging from 22h05m to 25h25m.

3.6.4.3 Dose documentation

The time of administration documented on the treatment chart was correct in only 61 (27.4%) infusions (Table 3.3). Of the 223 observed carbapenem infusions, 12 (5.4%) doses were not given (missed): these were signed off in the medication treatment chart as having been given, signing the time of administration as the expected scheduled time. An incorrect dose (one instead of two vials i.e., 1000mg instead of 2000mg Meropenem) was given on three (1.4%) occasions. These were signed off on the medication treatment chart as the expected prescribed dose.

3.6.4.4 Medication labelling of carbapenem infusion bags

One hundred and forty-four infusion bags (64.6%) were inspected. Although most retrieved infusion bags in the study displayed some medication information, this was variable. Over one

fifth (n=31, 21.5%) of infusion bags were left unlabelled. Unlabelled prepared infusions were left for varying periods of time before being administered, raising the risk of being administered to another patient. During tea and lunch breaks, nurses covering for the primary nurse ('buddy nurse') were unable to identify unlabelled infusion bags as the carbapenem dose; either infusing at the time or waiting in the bedspace to be commenced. Nurses wrote medication/patient details on 113 (78.5%) infusion bags; 75 (52.1%) infusion bags were marked with sticky labels and 38 (26.4%) with permanent marker written directly on the bags. Only 49 (34.0%) of the bags identified the patient for whom the drug was intended. Most of the infusion bags had the drug (110, 76.4%) and the dose (107, 74.3%) noted on the bag, however several bags had incorrect information about the type of carbapenem added to the bag, e.g., Meropenem written instead of Imipenem, 'antibiotic' instead of the drugs' name, or incorrect dose of drug. The most common details added onto carbapenem infusion bags were the time (61.8%) and date (55.6%) (Table 3.4). There was a significant (p 0.023) lower adherence rate to labelling of medication details on carbapenem infusion bags by ENs (7 of 14, 50.0%) compared with ICU trained RNs (19 of 24, 79.2%) and non-ICU trained RNs (87 of 106, 82.1%) (Table 3.5).

3.6.4.5 Comparison of labelling practices between public and private ICUs

Each study ICU had different expectations regarding labelling of intermittent medication infusion bags, with the public ICUs required to note the drug, dose, date and time by either permanent marker or the use of a plain sticker. Labelling practices differed between public and private ICUs, with nurses within the public ICUs using either plain labels (ICU A: 78.9%, p <0.001) or permanent markers (ICU B: 66.0%, p <0.001) to note medication details on the infusion bags. None of the infusion bags within the public ICUs had the patients' names noted on them, and this was explained as unnecessary by a shift leader due to the allocation of one RN per patient. Pre-printed sticky labels supplied to the private ICU required information such as: ward and bed number, drug batch and expiry date, and infusion fluid type and volume in addition to the patient's name, drug name and dose, date and time, and signatures of person mixing and administering the drug and the person checking the process. Despite the availability of, and ease of, these pre-printed stickers, this did not result in important patient and dose information, with less than 10 percent of bags including basic essential information (patient's name, drug, dose, date, time, and signature of nurse reconstituting the drug and administering the infusion). Although a permanent marker was

also used within the private ICU (ICU C: 6.4%), it was more common to use a pre-printed medication sticker or a patient hospital sticker (n=54, 69.2%). Only the private ICU nurses included the patients' name and hospital identification number on the infusion bags (ICU C: 62.8%, p <0.001, 95%CI: 51.1-73.5%) (Table 3.4). Essential information (patient's name, drug, dose, date, time, signature of nurse mixing and administering dose) was therefore found only in the private ICU (n=144, 8.3%), although only 12 labels in this unit included all required information There was therefore a significant difference between private (15.4%) and public ICUs (0%) (p <0.001) (Table 3.5).

3.6.4.6 Carbapenem infusion duration and compliance with written instructions

The duration of infusions was observed in 195 (of 223, 87.4%) administrations (Table 3.6). Two doses were given by bolus injection into the proximal port, 12 doses were not given and it was not possible to observe the completion of 14 infusions (transfer of patient to theatre/ward, or infusion not completed by the end of the observation period at 22h00). There were 78 (40%) incorrect infusion durations (non-compliance with instruction for infusion duration) including:

- 52 (66.7%) shortened durations, due to new line priming and setting the pump rate without accounting for the decreased bag volume post-priming
- 8 (10.3%) correct pump rates but incorrect choice of a fluid bag (100ml or 200ml bag instead of 50ml bag)
- 6 (7.7%) correct pump rates but incorrect choice of a small bag (50 ml bag instead of 100ml bag)
- 5 (6.4%) incorrect pump rate settings, resulting in undesired infusion duration
- 14 (17.9%) uncontrolled dose flow (open line), causing inappropriately rapid infusion

Protocols for infusion duration within the public ICUs were "*Meropenem diluted in 50mls NaCl and infused over three hours and imipenem diluted in 100 mls and infused over one hour*." Durations observed were; ICU A, meropenem: 15m to 4hr30m and ICU B, imipenem: 10m to 3hr. During the course of the study, no other carbapenems were used on the study patients in the two public ICUs. The ranges of infusion durations observed in ICU C were: meropenem: 10m to 2hr, doripenem infusions: 10m to 1hr, and ertapenem infusions: 15m to 1hr10m. Two doses were administered as bolus injections over 17 seconds and 1m respectively. Orders prescribed by clinicians in this unit superseded this guideline, but this occurred on only one occasion and in any

event was not adhered to. This stated that meropenem 2g should be administered over a duration of 3 hours; however, all doses observed (13 of 20, 65.0%) to this patient were administered between 10m and 1hr. One was administered by free flow infusion, with the nurse (EN) additionally repeatedly withdrawing the antibiotic from the distal port with a 10ml syringe and injecting this into the proximal port of the line over approximately 15 seconds until the medication bag was empty.

Although the literature advocates for prolonged carbapenem infusions for dose optimization, infusion durations were analysed according to compliance with written instructions available to the nurses (standing orders, hospital guidelines, or specific prescription orders). The public ICUs followed current literature for prolonged infusions, whereas the private ICU followed manufacturer instruction (seen in the hospital company's 'Intravenous Administration Guide' which appeared to follow drug packaging information). This was interesting for me as many of the anaesthetists/intensivists managing patients within the private ICU had relatively recently transitioned from the public healthcare sector into the private healthcare sector and one of these intensivists had in fact authored the standing orders for the two public study ICUs. The only clinician-prescribed duration instruction noted for a study patient (C4), was Meropenem administered over 3 hours. No other carbapenem prescriptions detailed duration instructions. In any event, the nurses administering the carbapenem infusions to patient C4 did not comply with the prescribed duration instruction and defaulted to 'unit practice' of 15–30-minute duration.

3.6.5 Calculation of carbapenem loss at preparation and administration phases

Volumetric analysis was conducted on all used equipment (vials, syringes, infusion bags and iv administration lines) retrieved at the patient's bedside when discarded. Fluid remaining in each item was measured and the antibiotic dose administered calculated from the remaining volume, expressed both as mg and percentage of the dose prescribed (Figure 1). The mean percentage loss at completion of the administration phase (in discarded infusion bags and lines, 40.1%, sd 18.8) of the infusion process was significantly greater ($p< 0.001$) than mean percentage loss (7.1%, sd 5.8) in discarded vials and syringes during the preparation phase, reflecting volume losses (Table 3.7). (It must be noted that the calculated percentage of antibiotic loss within infusion bags and infusion

administration line was affected by the percentage of antibiotic inserted into the infusion bags, therefore bag and line results should be considered with this in mind).

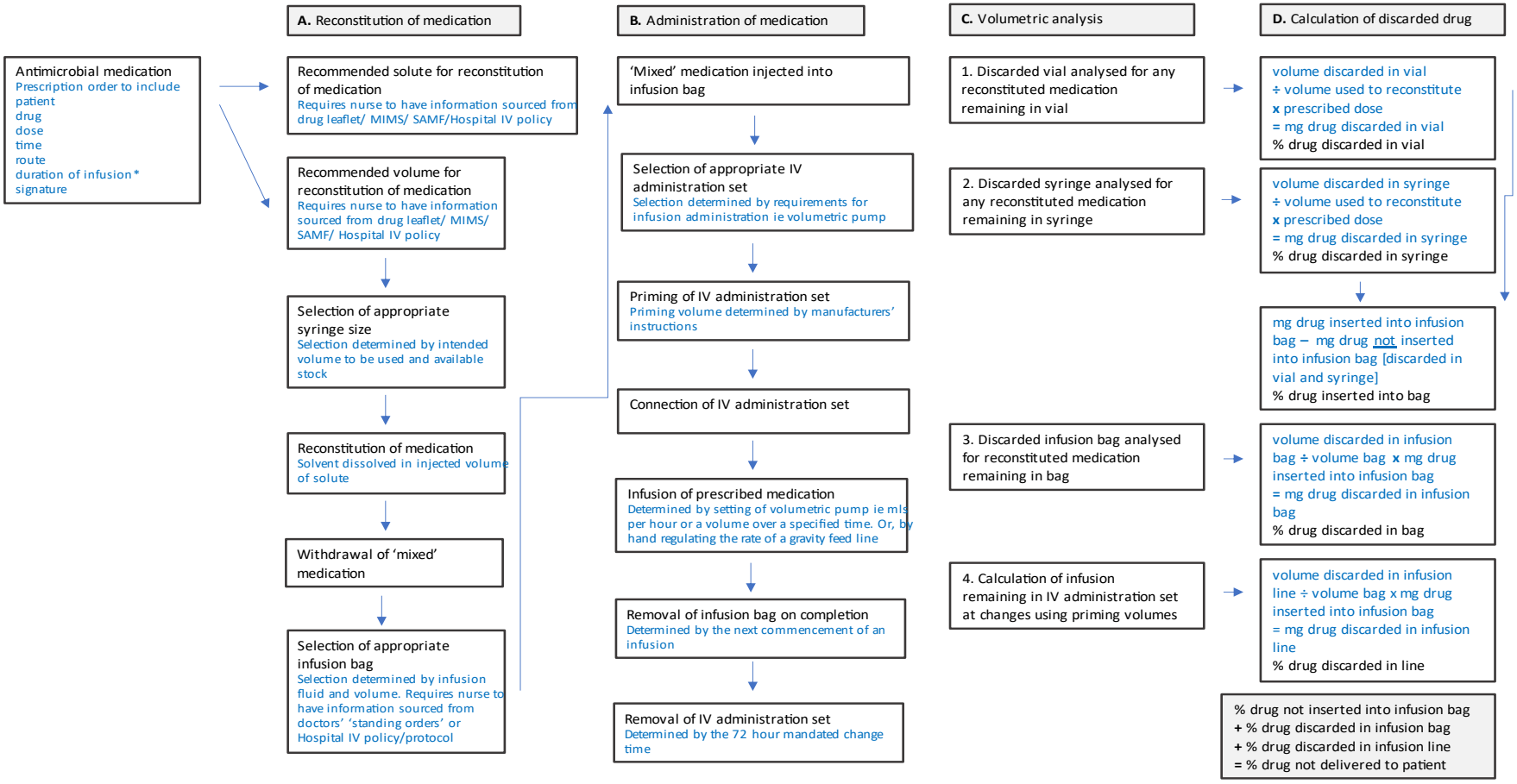
3.6.5.1 Retrieval of infusion items

Not all infusion items (vials, syringes, infusion bags, administration lines) could be retrieved from every dose administration. However, of seventeen (7.6%) doses where all four infusion items were able to be retrieved at the administration of the same dose, the total percentage antibiotic loss varied from 14.5% to 88.0% (median 52.4%, mean 50.0%, sd 20.3). Mean percentage of antibiotic dose not administered in *preparation items* (vials, syringes) retrieved at same dose administrations were 7.1% (range 0.0% – 28.0%, median 5.0% + sd 5.8). Analysis of percentage antibiotic not administered (mean 40.1%) to individual patients in *administration items* (infusion bags, administration lines) retrieved at same dose administrations were: min 9.5%, max 100%, median 32.5%, sd 18.8 ($p < 0.001$) (Table 3.8).

3.6.5.2 Dose preparation phase

During this phase, observations included; volume of diluent and syringe size used in drug dose reconstitution, choice of infusion bag volume, choice of administration infusion line, priming of line, and whether primary or secondary line. Carbapenem under-dosing resulted from process errors (incl. missed doses (12), incorrect number of vials reconstituted (3), and residual antibiotic discarded in vials and syringes. Of the 223 infusions; 137 vials (61.4%) and 94 syringes (42.2%) were retrieved for analysis. Measured volumes in *preparation items* showed mean losses of 4.9% and 1.2% in vials and syringes, respectively (Table 3.7).

Fig. 1. Calculation of carbapenem loss at preparation and administration phases



Information resources available in study units: MIMS (Monthly Index of Medical Specialities); SAMF (South African Medicines Formulary

All reconstitutions (100%) were carried out by the nurse allocated to the care of the patient. Sodium chloride (NaCl) was used for reconstituting all observed doses, mainly withdrawn from the NaCl bag intended for the medication dose. There were three occasions where NaCl vials were used for mixing the powder in the vial; two of which were 10ml NaCl vials, and one was a 10ml prefilled NaCl syringe. Loss of antibiotic dose was found from concentrated antibiotic discarded in small-volume syringes following reconstitution with an inadequate volume of diluent (53.4%). The choice of the size of syringe used for reconstitution and subsequent injection into infusion bags significantly affected the percentage of prescribed carbapenem dose in infusion bags: 5ml≤ syringes (mean 88.6% of prescribed dose), 10ml (mean 96.6%), and 20ml (mean 97.2%) (p 0.01) (Table 3.9).

Group comparisons demonstrated associations between residual carbapenem in discarded vials and nurse category, with a lower percentage of loss occurring with ICU-trained RNs (90.9%), compared with non-ICU-trained nurses (100%) (p 0.04), and between residual carbapenem discarded in syringes and shifts, with a higher proportion of loss occurring at night (86.1%) compared with day (67.2%) (p 0.041). Overall, insertion of an incomplete dose into the infusion bag (135 of 137, 98.5%) occurred less frequently with ICU-trained RNs (90.9%) (p 0.039). Reconstitution of an incorrect number of vials occurred three times (1.4%) and there were 12 (5.4%) missed doses with fewer missed doses on night shift (2.0% versus 8.2%) (p 0.04) (Table 3.10).

3.6.5.3 Dose administration phase

Residual volumes following infusion were measured from 144 retrieved used and discarded infusion bags. Irrespective of whether the volumetric pump was programmed for duration or volume administered, once the alarm sounded and the pump stopped, medication often remained in the infusion bag and was then discarded when the bag was removed for the next bag of medication. One hundred and twenty-two (84.7%) infusion bags, contained a measurable residual volume (mean loss, 7.5%, sd 9.5, median 3.6%, IQR 0.7-10.3). Fewer infusion bags managed by agency nurses (64.3%) than hospital employed nurses (89.1%) contained residual carbapenem in the private ICU (p 0.03) (Table 3.11).

The absence of flushing practice in any of the study sites inevitably led to large volumes of medication remaining in the administration lines discarded at routine line changes or when lines were discarded due to contamination. The use of small-volume infusion bags increases this loss considerably.[1,2,9,15,36,37] Eighty-two administration lines were analysed for residual volume (from 73 doses incl. volumetric with attached secondary infusion lines discarded at the same time during 'line change'). No syringe pumps were used in the administration of observed carbapenem infusions. Administration lines used to deliver carbapenem infusions were: 47 volumetric lines, 4 gravity feed lines, and 31 secondary lines (add-on-line) attached to volumetric (primary) lines (30 primary lines inactive). All discarded infusion administration lines contained undelivered (unflushed) antibiotic, the volume varying depending on the fluid level in the drip chamber (mean loss, 30.8%) (Table 3.7). Observations showed non-active flushing of residual carbapenem dose through the infusion line on completion of the dose i.e., infusion stopped but dose remaining in line. No *purposeful* flushing practices (i.e., deliberate clearing of the line (flushing)) with saline or maintenance fluid was observed following the carbapenem administrations (98.3%), although one patient had one dose administered using a secondary line attached to an *active* maintenance fluid line delivering a slow drip of fluid to '*keep vein open'*. One patient had two separate doses injected by syringe into the proximal port of a NaCl volumetric infusion line, which were then 'free flow' flushed from the line.

3.6.6 Analysis of infusion errors in the context of AMR

Underdosing of the amount of antimicrobial medication required for a therapeutic effect may mean that blood concentrations do not reach optimal MIC levels required to kill pathogens.[38,43-45] Of the twenty patients studied, only two patients received all observed doses at the scheduled time, and only four received all doses over the required infusion duration. Infusion practices (n=223, 100%) failed to deliver full-dose delivery of the prescribed medication. All patients were subject to loss of antibiotic (mean 29%/dose) in discarded infusion items. Rectal swabs were analysed by the National Health Laboratory Services (NHLS) and attending clinicians and Nursing Unit Managers were notified of identification of any CRE isolates.

3.6.6.1 Outcome measures (resistance, length of ICU stay and death)

Accepting that sample sizes were too small to make associations between under-dosing and patient outcomes (Table 3.12), individual patient data are presented with regard to identified MAEs and possible links with morbidity and mortality (Table 3.13). This was considered in the context of AMR - rectal swabs for CRE, and carbapenemases and multi-drug-resistant organisms (MDROs) in blood, ETAs, urine, and wound culture specimens. Future outcome measures were therefore AMR, LOS, and death. Antimicrobial resistance was identified in 13 (65%) patients in whom there was an average under-dosing of 32.1%. In total, carbapenemase-associated infections were identified from blood and other cultures in seven patients (35.0%), and multi-drug-resistant organisms (MDROs) were isolated from blood and other cultures in eight patients (40.0%). CRE was isolated from rectal swabs in 6 patients (30.0%) with 4 patients testing positive for CRE following commencement of carbapenem treatment. CRE was isolated in two patients before carbapenem treatment was commenced in the ICU, both of whom had been hospitalised in the previous week (previous carbapenem treatment was confirmed in one patient (C12). Fifteen patients had a length of stay (LOS) of 6 days or more (75.5%, sd 14.4), $\geq$6 (1st quartile) days. Three patients (n=20, 15.0%) B52, C4 and C12 died from unresolved sepsis; C4 and C12 had CRE-associated mortality; and carbapenemase were cultured in patients B 52 (day 5) and C12 (day 25). Six patients (30.0%) (C4, C5, C6, C8, C13, C22) did not have cultures taken while in ICU (ICU C) (Table 3.13).

3.6.6.2 Infusion errors

Infusion errors were categorised as those identified during observation of carbapenem doses administered to study patients, and those identified during volumetric analysis of the used and discarded infusion items (vials, syringes, infusion bags, and infusion lines). Comparisons were between: i) private and public hospital ICUs; ii) day and night shifts; iii) weekday and weekend/public holiday shifts; iv) ICU-trained and non-ICU-trained registered nurses (RN) and enrolled nurses (EN); and v) hospital-employed nurses and agency nurses (private ICU only).

Sampling of items of interest (n=1813) during observations of the 223 doses received by the 20 study patients revealed 950 various infusion errors (52.4%) (Table 3.14). These were: during day shifts (63.7%); during weekdays (64.1%); by non-ICU-trained RNs (70.7%); in the private ICU

(58.7%); and by hospital-employed nurses in the private ICU (74.8%). Errors were: missed carbapenem dose (5.4%); incorrect numbers of carbapenem vials reconstituted (1.4%); reconstitution of carbapenem vials with inadequate diluent (53.4%); inadequate labelling of patient and medication details on carbapenem infusion bags (91.7%); incorrect administration time of carbapenem dose (65.0%); incorrect spacing between carbapenem doses (65.0%); incorrect 'signing off' of dose administration time on medication chart (72.6%); incorrect compliance with duration of carbapenem infusion (40.0%); and non-active flushing of residual carbapenem dose through the infusion line on completion of the dose i.e., infusion bag now empty but dose remaining in line (98.3%) (Table 3.15). Loss of the antibiotic dose (mean %) was found in discarded equipment (vials 4.9%, syringes 1.2%, infusion bags 7.5%, and infusion lines 30.8%) (Table 3.7 & Table 3.16). Although it was only possible to retrieve all four infusion items on 17 doses, mean percentage of antibiotic loss to patients at same dose administration ranged from 28.5% to 74.5% (Table 3.17).

3.6.6.3 Staffing allocation

Staffing of the public ICUs was maintained at one ICU-trained registered nurse (RN)/one patient in ICU A, and one RN/one patient in ICU B. Staffing of the private ICU was seen to be a challenge with shift leaders spending large amounts of time trying to find agency nurses to complement the employed nursing staff. ICU-trained nurses (n=5) allocated to shift leader duties in this unit were also allocated for primary care of ill patients, in several cases delivering care to both a 'clean' (post cardiac surgery) and a patient who had been identified as CRE positive. The use of enrolled nurses (ENs) for primary patient care within specialist units in South Africa is prohibited by the South African Nursing Council.[42] However, it was noted that 39 carbapenem infusions in the private ICU were administered by enrolled nurses allocated to the care of patients as principal caregivers.

3.7 Rout publications relevant to this chapter

Please refer to papers listed below if interested

SUB-OPTIMAL DOSING

Rout J, Essack S, Brysiewicz P. Are nursing infusion practices delivering full-dose antimicrobial treatment? *J Antimicrob Chemother* 2019; 74(12):3418-3422. https://doi.org/10.1093/jac/dkz365

Rout J, Essack S, Brysiewicz P. Residual fluid after IV infusion drug administration: risk of suboptimal dosing. *Brit J Nurs* 2020; 29(2):S6-S7. https://doi.org/10.12968/bjon.2020.29.2.s6

Rout J, Brysiewicz P. Essack S. Antimicrobial infusion practices within intensive care units: Carbapenem infusion preparation and administration process errors. *Intens Crit Care Nurs* 2024; 86:103786. https://doi.org/10.1016/j.iccn.2024.103786

Rout J, Essack S. Nurses' antimicrobial infusion practice under the spotlight. *Br J Nurs* 2024; 33(14):S6-S7. https://doi.org/10.12968/bjon.2024.0148

Rout J, Brysiewicz P. Essack S. Management of residual volumes in intermittent medication infusions in hospital settings: A scoping review protocol. Accepted for publication. *Brit J Nurs* (2024).

DESCRIPTION OF ANTIMICROBIAL INFUSION DOCUMENTATION PRACTICES

Rout J, Essack S, Brysiewicz P, Evaluation of intermittent antimicrobial infusion documentation practices in intensive care units: A cross-sectional study. *Intens Crit Care Nurs* 2023; 79:103527. https://doi.org/10.1016/j.iccn.2023.103527

CHAPTER FOUR: RECOMMENDATIONS

Please note that these recommendations reflect developing evidence within the literature

4.1Antimicrobial stewardship

Attention should be given to all aspects of antibiotic preparation and administration particularly with consideration to the AMR challenges that currently face healthcare.[5,38,46]

Rationale: The way iv antimicrobial medications are administered may impact the efficacy of the drugs, and hence basic medication safety measures must be ensured by educating nurses about the link between AMS and AMR. ICU nursing often requires routine and repetitive activities, which, combined with a perceived low priority in a busy environment, can result in nurses rushing parts of the medication administration process so that they can get on with other duties perceived as more important.[47] Unfortunately, it is not always easy to link antimicrobial administration errors with selection pressure resulting in AMR, and nurses may not realise the long-term significance of these errors. Although this study examined carbapenem treatment administered to patients in ICUs, the concerns raised must apply to all patients receiving intermittent antimicrobial infusions and may help to partly explain the difficulty in reducing AMR in ICUs.

4.2 In-service training

Access to in-service training should be facilitated by hospital and unit management. Practical basic nursing skills must be reinforced including correct reconstitution of antimicrobials, administering the dose at the prescribed intervals, following instructions for the duration of the dose, and ensuring that the full dose has been administered by appropriate flushing following the dose.

Rationale: In order to provide optimum evidence-based care for the patient, the nurse needs to understand that the nursing role within AMS is aimed at the prevention of AMR. Safe conditions for patient care should be provided within ICUs, namely: supporting active AMS programmes to facilitate nurse understanding of the potential for AMR.[10,48-53]

4.3 Access to practice protocols and policies

Protocols, policies, guidelines and checklists should be made available by hospitals to guide clinical practice. Standard operating procedures (SOPs) should clarify the requirement to provide an antibiotic 'dedicated' administration line, flushing practices, and line changes

Rationale: These are important in ensuring patient safety.[1,5,14,17,54]

4.4 Medication safety measures

Nurses should be encouraged and supported to self-audit their practice. Self-reporting should be seen as a means of system improvement; but regular (monthly) audits of quality control measures should also be employed and monitored by senior ICU management.

Rationale: AMS best practice is founded on the principles of the right drug, the right dose, de-escalation when possible, and right duration.[55] Nurses are responsible for preparing and administering medication, and ensuring its correct and safe administration. They have a legal obligation to provide prescribed medication and that planned antimicrobial treatment reaches the patient, as ordered.[7,15]

4.5 Oversight of medication process

Be aware that shift leaders within the private sector ICU were often assigned patients, which made it almost impossible to oversee patient care in the rest of the unit. In addition, Nursing Unit Managers in all three ICUs, although available to the nurses assigned to patient care, were mostly tied up with administrative work and meetings.

Rationale: Not all shift leaders within the private sector ICU were ICU trained or had received 80 hours of instruction as required by the regulatory nursing body, South African Nursing Council (2021).[42] While ENs numbers were small, it is also concerning that ENs were assigned to primary care of patients. Additionally, the administration of iv medications should only be administered by RNs. The South African Nursing Council (2021)[42] prohibits the use of enrolled nurses (EN) for primary patient care within acute care areas such as ICUs.

4.6 Double-checking process

Double-checking is required for all parenteral medications irrespective of whether the full vial/ampoule dose is used, or a portion of the container has to be calculated for the prescribed dose. Steps expected are: i) correct drug (two nurses to check the vial/ampoule against the written prescription in the medication record); ii) drug due (two nurses to check the time of last dose administration in the medication record); iii) correct dosage (two nurses to confirm that the dosage contained in the vial/ampoule is correct, or to calculate and check that a withdrawn dose is correct); iv) patient identity (two nurses to confirm that the patient is the correct recipient of the drug by checking the ID band on the patient's wrist); and v) documentation to medication record (two nurses to sign the medication label and medication record).

Rationale: 'The lack of checking habits is considered to be one of the contributing factors for medication errors',[56] and was identified by the World Health Organization (2011)[57] as requiring attention during nurse pre-registration training.

4.7 Timing of dose

Nursing staff should be aware of the importance of avoiding missed or delayed doses of antimicrobials, which should be considered in the context of AMS.

Rationale: The patient's right to receive prescribed medication at the correct time is one of the well-accepted 'rights' of medication safety.[58-60] Such errors affect timing intervals and optimal dosing and may result in not achieving the required minimum inhibitory concentration (MIC), potentially resulting in AMR by not exposing the micro-organism to the drug for the necessary period of time.[45]

4.8 Documented time of dose administration

Time of dose administration should be documented accurately.

Rationale: The medication chart is an important historical and current record and supports communication during transfer of nursing care. Medication charts are medico-legal documents, and signing that a dose has been given correctly at the scheduled time when it has not been given at that time should be considered a fraudulent act.[61] Should the dose of medication be omitted for any reason, this should be noted on the medication chart.[62]

4.9 Medication labels on medication infusion bags

Basic safety requirements should be the patient's name and number, medication and dose, date and time, and signature of the nurse who has reconstituted the drug, injected it into the infusion bag, connected the bag to the administration set and commenced the infusion.

Rationale: Clear and accurate labelling of intermittent medication infusions reduces the potential for error and should be considered an essential part of medication administration. Morrow (2018)[7] states that any medication in a bag that is not labelled should be discarded and the preparation repeated. 'Drugs with the highest risk are those not administered immediately after preparation and the risk increases significantly if their labelling is not sufficiently clear'.[63]

4.10 Dose preparation phase

Care should be taken when reconstituting antimicrobial medications to use the recommended volume of diluent, preferably from a vial of sterile water for injection (or NaCl) and once mixed, to withdraw the reconstituted dose completely from the vial.

Rationale: Jarrett and colleagues (2023)[64] contend that variablility in the reconstitution of vials containing powder medication may contribute to AMR. Choice of syringe size (hence volume of diluent used to reconstitute the carbapenem) clearly affects the concentration of antibiotic withdrawn from vials to be injected into infusion bags, with consequent impact on dosage loss in discarded vials and syringes and the subsequent reduction in the amount of available carbapenem to be administered in the infusion bags.

4.11 Dose administration phase

Administration of an intermittent infusion should take into account the desired rate and duration of the infusion. Care should be taken to ensure that the infusion bag is empty and that the administration line has been flushed appropriately before considering that the infused dose is completed.

Rationale: If subtherapeutic levels of antimicrobial treatment are being used to manage an infection, it is more than likely that the pathogen will develop a resistance to the drug, rendering it useless.[3,9,11,19,65,66] Dose optimization is an important AMS strategy with the goal of curing the infection while reducing resistance due to sub-therapeutic drug exposure. Ensuring administration

of the full dose should be added to other important dose optimization considerations, such as patient characteristics (age, weight, renal function etc.), the causative organism, the site of infection, and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial medicine.[44,67]

4.12 Flushing lines

Nursing practices within AMS should also include judicious care with infusions of antimicrobial medicines, in particular, the use of a post-administration flush to complete the administration of a full dose.[1-19,34,35]

Rationale: Residual volume remains in the line until another dose is given, or discarded with line changes.[1-3,5,6,9,12-16,18-21] This leads to: underdosing of the medication or potential degradation of the medication (if left for long periods of time in the line).[37]

4.13 Flushing cautions

Flushing protocols should be aware of undesired rate of delivery of residual volume of medication intended for a prolonged infusion, and delivery of replacement medication such as Potassium Chloride (KCL) should the line not be a 'dedicated antibiotic' line.

Rationale: Residual medication may be administered unknowingly at the next infusion, or residual medication may be administered unknowingly at the undesired rate of the next new therapeutic fluid.[37]

4.14 Changing lines

There should be awareness of undelivered medication when considering IPC protocols which require that lines are discarded if considered contaminated. This includes 72 hr mandated changes for primary infusion lines, and 24 hr mandated changes for secondary lines. Be aware that nurses were also observed to discard lines when these were unlabelled, or when 'tidying up' before shift changes. Additional line changes may also occur following transfer of the patient from one department to another, for example, the movement of the patient from the emergency department or the operating room to the ICU in order to accommodate a change from gravity feed lines to infusion pump with resultant loss of therapeutic fluid.

Rationale: The Infusion Nurses Society (INS)[5] acknowledges that there is still confusion regarding line changes.[5] Current standard nursing recommendations are that continuous administration sets should be changed every 96 hours, (a change from the previously recommended period of 72 hours), primary intermittent administration sets should be discarded after 24 hours of use, and lines should be discarded immediately if contaminated.[68] Rickard and colleagues (2021)[69] further provide RCT evidence that this can safely be extended to 7 days.

CHAPTER FIVE: LIMITATIONS TO THE STUDY

5.1 General study limitations

- Although the study hospitals in this health district were deemed to be typical of public and private hospitals in the country, our findings may not be generalizable to ICUs with different patient or staffing profiles.
- Researchers at UKZN were instructed by the Biomedical Ethics Committee (BREC) to stop data collection following the commencement of a country-wide lockdown during the COVID-19 pandemic. Data collection was recommenced only a year later once conditions within the hospitals had stabilised.
- Observation periods of nursing practice were from 05h00-22h00 therefore administrations between 22h00 to 05h00 were not observed. Access to the public ICUs in the early mornings (05h00-08h00) and evenings (19h00-22h00) during the pandemic was restricted, impacting data collection in these ICUs during these times of the night shifts.
- Patients were not approached for enrollment or observed in the 'COVID-19 ICU' prior to admission to the main *Green* ICU (ICU C only).
- It must be acknowledged that when nurses know that they are under observation there is the potential for improved compliance through their heightened awareness during that particular aspect of care (the 'Hawthorne effect'), however the researcher was present on consecutive days for extended periods of time allowing a sense of 'belonging to the team' within the units.

5.2 Questionnaire limitations

- No existing KAP questionnaire had been found in the literature addressing the issues covered in this study, therefore an instrument had to be developed, and reviewed by ICU nursing experts prior to data collection, but was not validated by pre-testing in the intended study ICUs.
- The low KAP questionnaire response rate (42.9%) is also viewed as a limitation. Nursing management was variable during the study (ICU A: the Nursing Unit Manager went on extended leave during the first week of the study; ICU B: the Nursing Unit Manager retired in the second week of the study; and ICU C: the Nursing Unit Manager was situated in the COVID-19 ICU with the High Care Nursing Unit Manager overseeing the main ICU). Despite

shift leaders making numerous requests for return of questionnaires, the overall response rate did not improve.

- Nurses appeared to answer the questionnaires while they were working. It may have been better for nurses to have been allocated time off the unit, although this would have potentially compromised anonymity.
- The questionnaire was designed with 'mark the box' areas for responses and may have been better designed with options for written responses.
- The contradictory responses to some of the questions suggests that the questionnaire was hastily completed with insufficient attention given to reading the questions correctly. This may be attributed to no 'patient free' time being allocated by unit management to complete the questionnaires, or perhaps a lack of commitment to participate in the survey.
- Questionnaires posted together in the sealed response box on some shifts showed that identical errors had been made on the knowledge section, suggesting that respondents had asked each other for assistance. The low response rate and possible questionnaire vagaries may therefore, not provide a sound foundation for interpreting antimicrobial infusion results within the greater study.

5.3 Limitations of infusion observations

- Formulary restrictions in the public ICUs, thought to be due to cost constraints and concerns relating to AMS, may have impacted on numbers of enrolled patients receiving carbapenem treatment. During data collection (6 months), only 22 patients were placed on carbapenem treatment. Two patients were subsequently eliminated from analysis. The small number of patients (20) impacted inferential statistical analysis. Descriptive statistics, using frequency and percentage distributions, were therefore predominantly relied on to describe and summarise the data.
- Data collection was conducted by only one researcher (JR); therefore, it was not possible to observe every carbapenem infusion during observation periods, particularly when several study patients were receiving treatment at the same time in different parts of the ICU.
- Reconstitution of the antibiotic was sometimes difficult to observe as nurse position/movement occasionally obscured the volume of NaCl (withdrawn from the infusion bag) used to reconstitute the powder in the vial.

- Collecting used and discarded syringes and vials, for volumetric analysis of residual antibiotic, was sometimes difficult as the nurses' automatic practice was to discard these into sharps containers.
- The collection of administration lines was also difficult as they were not always changed during observation periods.

5.4 Outcome measure limitations

- There were different approaches to taking cultures in the public and private ICUs. On admission to the public ICUs, all patients had a series of cultures - endotracheal aspirate (ETA) (and sputum if not intubated), urine, blood, and wound exudate. However, this was not the routine in the private ICU, where cultures were ordered by clinicians only if deemed necessary.
- Unfortunately, there were several submitted rectal swabs which could not be found on the NHLS Labtrak database and were therefore lost to the study, and several results which reported 'lab error'.

CHAPTER SIX: CONCLUSION

The importance of using best administration practices of iv antimicrobial medicines is gaining recognition in meeting the challenge of dose optimization as a tool to slow the development of drug-resistant bacteria. To our knowledge, this is the first study that has focused strictly on the procedural administration of antimicrobial infusions. Less than 50% of respondents reported receiving teaching on AMS during pre-registration training and since qualifying as a nurse. In this observational study conducted over three ICUS, the preparation and administration of carbapenem agents (ertapenem, meropenem, imipenem and doripenem) was poor, suggesting inadequately trained nurses. Although this study focused on carbapenem treatment, the level of nursing errors is concerning as it evidences general suboptimal quality of care in these ICUs, particularly in a patient population that probably lacks the physiological reserve to tolerate additional injury. Furthermore, it is also concerning that these errors were either unnoticed or ignored as deviations from expected practice by ICU shift leaders, ICU unit managers, doctors, or pharmacists. The infusion errors noted on this study were not identified as errors by: i) the primary nurse assigned to the patient and administering the dose; ii) the nurse double-checking the dose with the primary nurse; iii) the shift leader; iv) the nursing unit manager; v) the doctor managing the patient; (vi) the pharmacist (if present in the unit); (vii) or the clinical nursing facilitator (if present in the unit).

Every aspect of drug administration required improvement and has significance in sub-optimal delivery of carbapenem treatment. Inadequate double-checking resulted in missed and incorrect doses, and timing errors; impacting intended dose management and prescribed dosing intervals. Safety mechanisms that have been put in place to reduce iv medication errors, therefore, seemed to be a ‘paper exercise’ within this study, with nurses carrying the medication label to another nurse to countersign. This was a common occurrence and meant that the nurse ‘checking’ did not receive an opportunity to identify the patient for whom the dose was intended, or to read and confirm the medication order, or view the medication vial, diluent and bag of infusion fluid. Deviations from safety procedures may also result in undesired variations in dosing intervals. This casual attitude towards dose checking creates an environment where a safety net of ‘catching’ errors is lost prior to the final stage of the medication process. Documentation in the medication treatment chart did not reflect the actual administrations and should be considered a serious breach of nursing ethics.

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TABLES

Table 2.1 Inclusion and exclusion criteria

Inclusion criteria	• All nurses allocated to patient care/shift leading duties in the study ICUs • All nurses working day/night shift duties • All nurses registered/enrolled with the South African Nursing Council • All nurses employed by the study hospital on a permanent/part-time basis • All nurses engaged by the study hospital, as agency temporary nurses
Exclusion criteria	• Enrolled Nursing Auxiliary nurses • Caregivers

Table 2.2 Results of ICU nurse knowledge, attitude and practice questionnaire

		Total	ICU A	ICU B	ICU C
Response rate		69 [n161, 42.9%]	25 [n33, 75.8%]	28 [n76, 36.8%]	16 [n52, 30.8%]
Age	1 20-29	7 [10.1%]	0 [0.0%]	6 [21.4%]	1 [6.3%]
	2 30-39	24 [34.8%]	5 [20.0%]	11 [39,3%]	8 [50.0%]
	3 40-49	18 [26.1%]	9 [36.0%]	7 [25.0%]	2 [12.5%]
	4 50-59	14 [20.3%]	9 [36.0%]	3 [10.7%]	2 [12.5%]
	5 60-65	4 [5.8%]	1 [4.0%]	1 [3.6%]	2 [12.5%]
	No response	2 [2.9%]	1 [4.0%]	0 [0.0%]	1 [6.3%]
Qualification *Additional qualification	1 Enrolled nurse	4 [5.8%]	1 [4.0%]	0 [0.0%]	3 [18.8%]
	2 RN diploma	55 [79.7%]	22 [88.0%]	21 [75.0%]	12 [75.0%]
	3 RN degree	8 [11.6%]	2 [8.0%]	5 [17.9%]	1 [6.3%]
	4 ICU diploma*	37 [53.6%]	24 [96.0%]	8 [28.6%]	5 [31.3%]
	No response	2 [2.9%]	0 [0.0%]	2 [7.1%]	0 [0.0%]
Year obtained nursing qualification	1980-1989	5 [7.2%]	1 [4.0%]	2 [7.1%]	1 [6.3%]
	1990-1999	6 [8.7%]	2 [8.0%]	0 [0.0%]	3 [18.8%]
	2000-2009	14 [20.3%]	11 [27.5%]	2 [7.1%]	1 [6.3%]
	2010 to 2020	31 [44.9%]	3 [12.0%]	19 [67.9%]	9 [56.3%]
	no answer	13 [18.8%]	8 [32.0%]	5 [17.9%]	2 [12.5%]
Year obtained ICU qualification	1980-1989	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
	1990-1999	2 [2.9%]	2 [8.0%]	0 [0.0%]	0 [0.0%]
	2000-2009	16 [23.2%]	12[48.0%]	3 [10.7%]	1 [6.3%]
	2010 to 2020	19 [27.5%]	10 [40.0%]	6 [21.4%]	3 [18.8%]
	no answer	32 [46.4%]	1 [4.0%]	19 [67.9%]	12 [75.0%]
Employed by hospital	1 Fulltime	60 [87.0%]	23 [92.0%]	28 [100%]	9 [56.3%]
	2 Part time	1 [1.4%]	0 [0.0%]	0 [0.0%]	1 [6.3%]
	No response	8 [11.6%]	2 [8.0%]	0 [0.0%]	6 [37.5%]
Agency	1 Regular booking at hospital	5 [7.2%]	0 [0.0%]	0 [0.0%]	5 [31.3%]
	2 Occasional booking by hospital	1 [1.4%]	0 [0.0%]	0 [0.0%]	1 [6.3%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
1. Did your training include information on antibiotic medicines?	1 no	2 [2.9%]	0 [0.0%]	2 [7.1%]	0 [0.0%]
	2 a lot	12 [17.4%]	4 [16.0%]	2 [7.1%]	6 [37.5%]
	3 a little	16 [23.2%]	2 [8.0%]	9 [32.1%]	5 [31.3%]
	4 yes	38 [55.1%]	18 [72.0%]	15 [53.6%]	5 [31.3%]
	No response	1 [1.4%]	1 [4.0%]	0 [0.0%]	0 [0.0%]
2. Did you have education on IV injections during your training?	1 yes	58 [84.1%]	23 [92.0%]	21 [75.0%]	14 [87.5%]
	2 sometimes	6 [8.7%]	1 [4.0%]	4 [14.3%]	1 [6.3%]
	3 no	3 [4.3%]	0 [0.0%]	2 [7.1%]	1 [6.3%]
	4 can't remember	1 [1.4%]	0 [0.0%]	1 [3.6%]	0 [0.0%]
	No response	1 [1.4%]	1 [4.0%]	0 [0.0%]	0 [0.0%]
3. Did you have practical training on intravenous infusions before you qualified?	1 no	12 [17.4%]	2 [8.0%]	7 [25.0%]	3 [18.8%]
	2 yes	50 [72.5%]	19 [76.0%]	20 [71.4%]	11 [68.8%]
	3 can't remember	5 [7.2%]	2 [8.0%]	1 [3.6%]	2 [12.5%]
	4 sometimes	1 [1.4%]	1 [4.0%]	0 [0.0%]	0 [0.0%]
	No response	1 [1.4%]	1 [4.0%]	0 [0.0%]	0 [0.0%]
4. a) Amoxicillin is a… [multiple answers possible]	1 cephalosporin	1 [1.4%]	1 [4.0%]	0 [0.0%]	0 [0.0%]
	2 antibiotic	46 [66.7%]	21 [84.0%]	11 [39.3%]	14 [87.5%]
	3 penicillin	36 [52.2%]	9 [36.0%]	15 [53.6%]	12 [75.0%]
	No response	9 [13.0%]	2 [8.0%]	6 [21.4%]	1 [6.3%]
b) Zinacef is a…	1 carbapenem	6 [8.7%]	2 [8.0%]	2 [7.1%]	2 [12.5%]
	2 cephalosporin	43 [62.3%]	17 [68.0%]	13 [46.4%]	13 [81.3%]
	3 echinocandin	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
	No response	20 [29.0%]	6 [24.0%]	13 [46.42%]	1 [6.3%]
c) Carbapenems include…	1 Rocephin	11 [15.9%]	4 [16.0%]	7 [25.0%]	0 [0.0%]
	2 ertapenem	44 [63.8%]	17 [68.0%]	14 [50.0%]	13 [81.3%]
	3 antifungal	4 [5.8.0%]	1 [4.0%]	2 [7.1%]	1 [6.3%]
	No response	12 [17.4%]	4 [16.0%]	6 [21.4%]	2 [12.5%]
d) Meropenem is a…	1 narrow spectrum	5 [7.2%]	1 [4.0%]	3 [10.7%]	1 [6.3%]
	2 cephalosporin	9 [13.0%]	5 [20.0%]	3 [10.7%]	1 [6.3%]
	3 carbapenem	40 [58.0%]	15 [60.0%]	12 [42.9%]	13 [81.3%]
	No response	15 [21.7%]	4 [16.0%]	10 [35.7%]	1 [6.3%]
e) Augmentin contains…	1 antibiotic	27 [39.1%]	10 [40.0%]	6 [21.4%]	11 [68.8%]

[multiple answers possible]	2 clavulanic acid	29 [42.0%]	13 [52.0%]	10 [35.7%]	6 [37.5%]
	3 beta-lactamase inhibitor	7 [10.1%]	3 [12.0%]	2 [7.1%]	2 [12.5%]
	No response	16 [23.2%]	4 [16.0%]	11 [39.3%]	1 [6.3%]
5. How have you given antibiotics to patients? [multiple answers possible]	1 PO	50 [72.5%]	18 [72.0%]	18 [64.3%]	14 [87.5%]
	2 IM	32 [46.4%]	8 [32.0%]	14 [50.0%]	10 [62.5%]
	3 IV	64 [92.8%]	24 [96.0%]	27 [96.4%]	13 [81.3%]
	4 Infusion	45 [65.2%]	16 [64.0%]	18 [64.3%]	11 [68.8%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
6. Do you feel confident giving IV antibiotics to a patient?	1 sometimes	3 [4.3%]	1[4.0%]	2 [7.1%]	0 [0.0%]
	2 no	2 [2.9%]	1[4.0%]	0 [0.0%]	1 [6.3%]
	3 yes	56 [81.2%]	21 [84.0%]	25 [89.3%]	10 [62.5%]
	4 always	8 [12.0%]	2 [8.0%]	1 [3.6%]	5 [31.3%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
7. When you give an IV antibiotic do you refer to any of the following for guidance? [multiple answers possible]	1 pharmacist	22 [31.9%]	8 [32.0%]	5 [17.9%]	9 [56.3%]
	2 policy file	27 [39.1%]	8 [32.0%]	11 [39.3%]	8 [50.0%]
	3 ICU 'buddy'	31 [44.9%]	9 [36.0%]	11 [39.3%]	11 [68.8%]
	4 MIMS	19 [27.5%]	7 [28.0%]	3 [10.7%]	9 [56.3%]
	5 SAMF	10 [14.5%]	6 [24.0%]	3 [10.7%]	1 [6.3%]
	6 Package insert	47 [68.1%]	17 [68.0%]	18 [64.3%]	12 [75.0%]
	7 Doctor	41 [59.4%]	15 [60.0%]	17 [60.7%]	9 [56.3%]
	8 ICU shift leader	38 [55.1%]	8 [32.0%]	18 [64.3%]	12 [75.0%]
	9 ICU unit manager	23 [33.3%]	6 [24.0%]	15 [53.6%]	2 [12.5%]
	10 other	3 [4.3%]	1[4.0%]	2 [7.1%]	0 [0.0%]
	No response	1 [1.4%]	1[4.0%]	0 [0.0%]	0 [0.0%]
8. How often do you need advice with giving an IV antibiotic?	1 often	14 [20.3%]	3 [12.0%]	5 [17.9%]	6 [37.5%]
	2 not often	15 [21.7%]	5 [20.0%]	7 [25.0%]	3 [18.8%]
	3 never	4 [5.8%]	1[4.0%]	1 [3.6%]	2 [12.5%]
	4 sometimes	36 [52.2%]	16 [64.0%]	15 [53.6%]	5 [31.3%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
9. Where is the hospital IV antibiotic policy kept? [multiple answers possible]	1 there isn't one	6 [8.7%]	4 [16.0%]	2 [7.1%]	0 [0.0%]
	2 in the duty room	39 [56.5%]	15 [60.0%]	10 [35.7%]	14 [87.5%]
	3 in the patient's file	14 [20.3%]	3 [12.0%]	8 [28.6%]	3 [18.8%]
	4 on the medication trolley	2 [2.9%]	2 [8.0%]	0 [0%]	0 [0.0%]
	5 other	14 [20.3%]	2 [8.0%]	11 [39.3%]	1 [6.3%]
	No response	5 [7.2%]	2 [8.0%]	2 [7.1%]	1 [6.3%]
10. Do you find the hospital IV antibiotic policy useful?	1 no	3 [4.3%]	1 [4.0%]	0 [0.0%]	2 [12.5%]
	2 yes	44 [63.8%]	19 [76.0%]	14 [50.0%]	11 [68.8%]
	3 sometimes	10 [14.5%]	0 [0.0%]	7 [25.0%]	3 [18.8%]
	4 I have never seen this policy	9 [13.0%]	5 [20.0%]	4 [14.3%]	0 [0.0%]
	No response	3 [4.3%]	0 [0.0%]	3 [10.7%]	0 [0.0%]
11. Did you have teaching on antimicrobial stewardship during your nursing training?	1 yes	31 [44.9%]	6 [24.0%]	14 [50.0%]	11 [68.8%]
	2 I can't remember	11 [15.9%]	3 [12.0%]	7 [25.0%]	1 [6.3%]
	3 sometimes	3 [4.3%]	0 [0.0%]	3 [10.7%]	0 [0.0%]
	4 no	24 [34.8%]	16 [64.0%]	4 [14.3%]	4 [25.0%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
12. Have you had antimicrobial stewardship training since you qualified?	1 yes	32 [46.4%]	6 [24.0%]	14 [50.0%]	12 [75.0%]
	2 no	31 [44.9%]	16 [64.0%]	11 [39.3%]	4 [25.0%]
	3 not sure	6 [8.7%]	3 [12.0%]	3 [10.7%]	0 [0.0%]
	4 frequently	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
13. How often do you have antimicrobial stewardship training?	1 once a year	23 [33.3%]	2 [8.0%]	10 [35.7%]	11 [68.8%]
	2 once a month	9 [13.0%]	2 [8.0%]	5 [17.9%]	2 [12.5%]
	3 once a week	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
	4 once a day	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
	5 never	34 [49.3%]	20 [80.0%]	11 [39.3%]	3[18.8%]
	No response	3 [4.3%]	1[4.0%]	2 [7.1%]	0 [0.0%]
14. Who gives you the antimicrobial stewardship training? [multiple answers possible]	1 clinical facilitator	20 [29.0%]	1[4.0%]	10 [35.7%]	9 [56.3%]
	2 ICU unit manager	31 [44.9%]	4 [16.0%]	25 [89.3%]	2 [12.5%]
	3 shift leader	12 [17.4%]	1[4.0%]	3 [10.7%]	8 [50.0%]
	4 IPC nurse	15 [21.7%]	8 [32.0%]	2 [7.1%]	5 [31.3%]
	No response	22 [31.9%]	13 [52.0%]	8 [28.6%]	1[6.3%]
	1 microbiologist	8 [11.6%]	3 [12.0%]	3 [10.7%]	2 [12.5%]

15. Do you get antimicrobial stewardship training from any of the people listed below? [multiple answers possible]	2 pharmacist	19 [27.5%]	5 [20.0%]	8 [28.6%]	6 [37.5%]
	3 doctors	23 [33.3%]	14 [56.0%]	7 [25.0%]	2 [12.5%]
	4 other	11 [15.9%]	6 [24.0%]	4 [14.3%]	1 [6.3%]
	No response	8 [11.6%]	3 [12.0%]	4 [14.3%]	1 [6.3%]
16. Where do you have this antimicrobial stewardship training? [multiple answers possible]	1 at the bedside	26 [37.7%]	9 [36.0%]	8 [28.6%]	9 [56.3%]
	2 in the duty room	19 [27.5%]	8 [32.0%]	3 [10.7%]	8 [50.0%]
	3 in the training room	8 [11.6%]	1[4.0%]	6 [21.4%]	1 [6.3%]
	4 I am sent to congresses	4 [5.8%]	3 [12.0%]	1 [3.6%]	0 [0.0%]
	5 other	6 [8.7%]	4 [16.0%]	2 [7.1%]	0 [0.0%]
	No response	15 [21.7%]	5 [20.0%]	8 [28.6%]	2 [12.5%]
17. Have you had training on IV administration of antibiotic medications in this hospital? [multiple answers possible]	1 yes	30 [43.5%]	11 [44.0%]	10 [35.7%]	9 [56.3%]
	2 in-service	21 [30.4%]	5 [20.0%]	8 [28.6%]	8 [50.0%]
	3 on induction	10 [14.5%]	3 [12.0%]	7 [25.0%]	0 [0.0%]
	4 no	17 [24.6%]	11 [44.0%]	4 [14.3%]	2 [12.5%]
	No response	2 [2.9%]	0 [0.0%]	1 [3.6%]	1 [6.3%]
18. Who gives you this training? [multiple answers possible]	1 drug rep	11 [15.9%]	2 [8.0%]	0 [0.0%]	9 [56.3%]
	2 doctor	17 [24.6%]	12 [48.0%]	2 [7.1%]	3 [18.8%]
	3 shift leader	11 [15.9%]	4 [16.0%]	2 [7.1%]	5 [31.3%]
	4 clinical facilitator	24 [34.8%]	2 [8.0%]	19 [67.9%]	3 [18.8%]
	5 other	12 [17.4%]	9 [36.0%]	3 [10.7%]	0 [0.0%]
	No response	10 [14.5%]	4 [16.0%]	3 [10.7%]	3 [18.8%]
19. Who instructs you on what size (volume) infusion bag to mix the antibiotic in? [multiple answers possible]	1 shift leader	14 [20.3%]	5 [20.0%]	5 [17.9%]	4 [25.0%]
	2 pharmacist	18 [26.1%]	6 [24.0%]	3 [10.7%]	9 [56.3%]
	3 doctor	41 [59.4%]	22 [88.0%]	14 [50.0%]	5 [31.3%]
	4 clinical facilitator	10 [14.5%]	2 [8.0%]	7 [25.0%]	1 [6.3%]
	5 SOP	17 [24.6%]	9 [36.0%]	3 [10.7%]	5 [31.3%]
	6 other	14 [20.3%]	6 [24.0%]	4 [14.3%]	4 [25.0%]
	No response	3 [4.3%]	0 [0.0%]	2 [7.1%]	1 [6.3%]
20. How do you administer the antibiotic infusion? [multiple answers possible]	1 gravity feed giving set	9 [13.0%]	4 [16.0%]	5 [17.9%]	0 [0.0%]
	2 infusion pump	62 [89.9%]	22 [88.0%]	24 [85.7%]	16 [100%]
	3 syringe pump	22 [31.9%]	6 [24.0%]	13 [46.4%]	3 [18.8%]
	4 smart pump	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]
21. Who instructs you on which equipment to use? [multiple answers possible]	1 pharmacist	2 [2.9%]	1[4.0%]	0 [0.0%]	1 [6.3%]
	2 clinical facilitator	19 [27.5%]	1[4.0%]	12 [42.9%]	6 [37.5%]
	3 shift leader	20 [29.0%]	6 [24.0%]	7 [25.0%]	7 [43.8%]
	4 doctor	26 [37.7%]	15 [60.0%]	7 [25.0%]	4 [25.0%]
	5 SOP	16 [23.2%]	9 [36.0%]	2 [7.1%]	5 [31.3%]
	6 other	11 [15.9%]	5 [20.0%]	3 [10.7%]	3 [18.8%]
	No response	3 [4.3%]	1[4.0%]	1 [3.6%]	1 [6.3%]
22. When is the IV antibiotic administration giving set changed? [multiple answers possible]	1 when it is contaminated	13 [18.8%]	7 [28.0%]	4 [14.3%]	2 [12.5%]
	2 when the antibiotic infusion course is finished	5 [7.2%]	1[4.0%]	2 [7.1%]	2 [12.5%]
	3 when changing from gravity to infusion pump sets	1 [1.4%]	0 [0.0%]	1 [3.6%]	0 [0.0%]
	4 every 72 hours	57 [82.6%]	24 [96.0%]	24 [85.7%]	9 [56.3%]
	5 other	5 [7.2%]	0 [0.0%]	2 [7.1%]	3 [18.8%]
	No response	5 [7.2%]	1[4.0%]	1 [3.6%]	3 [18.8%]
23. Do you use the iv antibiotic infusion line to administer other medications ie Perfalgan/ KCL as well as antibiotics?	1 yes	24 [34.8%]	11 [44.0%]	9 [32.1%]	4 [25.0%]
	2 sometimes	7 [10.1%]	1 [4.0%]	4 [14.3%]	2 [12.5%]
	3 no	35 [50.7%]	12 [48.0%]	15 [53.6%]	8 [50.0%]
	4 I'm not sure	1 [1.4%]	0 [0.0%]	0 [0.0%]	1 [6.3%]
	No response	2 [2.9%]	1 [4.0%]	0 [0.0%]	1 [6.3%]
24. Do you clear the line of the other medication before giving an antibiotic infusion?	1 sometimes	6 [8.7%]	2 [8.0%]	3 [10.7%]	1 [6.3%]
	2 no	16 [23.2%]	5 [20.0%]	5 [17.9%]	6 [37.5%]
	3 under special circumstances	7 [10.1%]	3 [12.0%]	1 [3.6%]	3 [18.8%]
	4 yes	39 [56.5%]	15 [60.0%]	18 [64.3%]	6 [37.5%]
	No response	1 [1.4.0%]	0 [0.0%]	1 [3.6%]	0 [0.0%]
25. What would you like more education and training on?	1 different groups of antibiotics	42 [60.9%]	13 [52.0%]	16 [57.1%]	13 [81.3%]
	2 antifungals	16 [23.2%]	5 [20.0%]	5 [17.9%]	6 [37.5%]
	3 how to give antibiotic infusions	11 [15.9%]	2 [8.0%]	4 [14.3%]	5 [31.3%]

[multiple answers possible]	4 antimicrobial resistance	45 [65.2%]	19 [76.0%]	17 [60.7%]	9 [56.3%]
	5 other	3 [4.3%]	1 [4.0%]	1 [3.6%]	1 [6.3%]
	No response	0 [0.0%]	0 [0.0%]	0 [0.0%]	0 [0.0%]

Table 2.3 Antibiotic group knowledge (Q.4)

Respondents n=69		a) Amoxicillin is a… *penicillin*	b) Zinacef is a… *cephalosporin*	c) Carbapenems include… *Ertapenem*	d) Meropenem is a… *carbapenem*	e) Augmentin contains… *clavulanic acid*
Correct answer		36 [n=60, 60.0%]	43 [n=49, 87.8%]	44 [n=57, 77.2%]	40 [n=54, 74.1%]	29 [n=53, 54.7%]
Incorrect answer		24 [n=60, 40.0%]	6 [n=49, 12.2%]	13 [n=57, 22.8%]	14 [n=54, 25.9%]	24 [n=53, 45.3%]
No answer		9 [n=69, 13.0%]	20 [n=69, 29.0%]	12 [n=69, 17.4%]	15 [n=69, 21.7%]	16 [n=69, 23.2%]
Hospitals n=69	Private n=16	12 [n=16, 75.0%]	13 [n=16, 81.3%]	13 [n=16, 81.3%]	13 [n=16, 81.3%]	6 [n=16, 37.5%]
	Public n=53	24 [n=53, 45.3%]	30 [n=53, 56.6%]	31 [n=53, 58.5%]	27 [n=53, 50.9%]	23 [n=53, 43.4%]
	p values	0.048	0.09	0.14	0.043	0.78
Years of nursing experience n=56	>10 years n=25	14 [n=25, 56.0%]	18 [n=25, 72.0%]	21 [n=25, 84.0%]	17 [n=25, 68.0%]	17 [n=25, 68.0%]
	<10 years n=31	18 [n=31, 58.1%]	17 [n=31, 54.8%]	17 [n=31, 54.8%]	16 [n=31, 51.6%]	8 [n=31, 25.8%]
	p values	0.247	0.45	0.02	0.45	0.004
Qualifications n=69	ICU trained n=29	11 [n=29, 37.9%]	20 [n=29, 69.0%]	19 [n=29, 65.5%]	18 [n=29, 62.1%]	15 [n=29, 51.7%]
	non-ICU trained n=36	22 [n=36, 61.1%]	20 [n=36, 55.6%]	21 [n=36, 58.3%]	20 [n=36, 55.6%]	14 [n=36, 38.9%]
	EN n=4	3 [n=4, 75.0%]	3 [n=4, 75.0%]	4 [n=4, 100%]	2 [n=4, 50.0%]	0 [n=4, 0%]
	p values	0.139	0.51	0.34	0.86	0.13
Nurses with advanced training n=65	RN with ICU training and/or degree n=39	19 [n=39, 48.7%]	27 [n=39, 69.2%]	27 [n=39, 69.2%]	25 [n=39, 64.1%]	21 [n=39, 53.8%]
	RN n=26	14 [n=26, 53.8%]	13 [n=26, 50.0%]	13 [n=26, 50.0%]	13 [n=26, 50.0%]	8 [n=26, 30.8%]
	p values	0.80	0.13	0.13	0.31	0.08
*Private healthcare sector only n=16	Hospital employed nurses* n=10	9 [n=10, 90.0%]	10 [n=10, 100%]	9 [n=10, 90.0%]	9 [n=10, 90.0%]	5 [n=10, 50.0%]
	Agency nurses* n=6	3 [n=6, 50.0%]	3 [n=6, 50.0%]	4 [n=6, 66.7%]	4 [n=6, 66.7%]	1 [n=6, 16.7%]
	p values	0.12	0.036	0.52	0.52	0.31

Table 2.4. Flushing infusion line between doses (Q.24)

Responses		Yes	No/sometimes
Hospitals n=69	Private hospital n=16	6 [n=16, 37.5%]	10 [n=16, 62.5%]
	Public hospital n=53	33 [n=53, 62.3%]	19 [n=53, 35.8%]
	p values	0.086	
Years of nursing experience n=56	>10 years n=25	15 [n=25, 60.0%]	10 [n=25, 40.0%]
	<10 years n=31	19 [n=31, 61.3%]	12 [n=31, 38.7%]
	p values	1.00	
Qualifications n=69	ICU trained n=29	18 [n=29, 62.1%]	11 [n=29, 37.9%]
	Non-ICU trained n=36	19 [n=36, 52.8%]	16 [n=36, 44.4%]
	Enrolled nurse n=4	2 [n=4, 50.0%]	2 [n=4, 50.0%]
	p values	0.794	
Advanced training n=65	RN with ICU training and/or degree n=39	25 [n=39, 64.1%]	14 [n=39, 35.9%]
	RN n=26	12 [n=26, 46.2%]	13 [n=26, 50.0%]
	p values	0.30	
*Private healthcare sector only n=16	Hospital employed nurses* n=10	2 [n=10, 20.0%]	8 [n=10, 80.0%]
	Agency nurses* n=6	4 [n=6, 66.7%]	2 [n=6, 33.3%]
	p values	0.12	

Table 3.1 ICU and patient demographics

		ICU A	ICU B	ICU C
Hospital	n=3	Regional public hospital	Tertiary public hospital	Private hospital
ICU characteristics	n=3	Closed ICU admitting adults and children over 12 years [6 beds]	Closed ICU admitting adults [15 beds]	Open ICU admitting all ages [10 beds]
Nurse staffing		One ICU-trained nurse/ICU patient. Additional ICU trained nurse as shift leader	One registered general nurse/ICU patient. An ICU-trained nurse as shift leader	One nurse/ two patients. Mixed skill set using hospital and agency nurses [i.e., ICU-trained nurses/ registered general nurses/ enrolled nurses]
Study patients	n=105	31 [n=105, 29.5%]	52 [n=105, 49.5%]	22 [n=105, 21.0%]
Patients treated with carbapenems	20 [n=105, 19.0%]	3 [n=31, 9.7%]	8 [n=52, 15.9%]	9 [n=22, 40.9%]
Observation period	184 days	53 [n=184, 28.8%]	56 [n=184, 30.4%]	75 [n=184, 40.8%]
Observation doses	n=223	29 [n=223, 13.0%]	63 [n=223, 28.3%]	131 [n=223, 58.7%]
Carbapenem Rx	Meropenem courses 12 [n=25, 48.0%]	3 [n=12, 25.0%]	0 [n=12, 0.0%]	9 [n=12, 75.0%]
	Imipenem courses 10 [n=25, 40.0%)	0 [n=10, 0.0%]	10 [n=10, 100%)	0 [n=10, 0.0%]
	Doripenem courses 1 [n=25, 4.0%]	0 [n=1, 0.0%]	0 [n=1, 0.0%]	1 [n=1, 100%]
	Ertapenem courses 2 [n=25, 8.0%]	0 [n=2, 0.0%]	0 [n=2, 0.0%]	2 [n=2, 100%]
Gender	Male n=13 [n=20, 65.0%]	3 [n=13, 23.1%]	5 [n=13, 38.5%]	5 [n=13, 38.5%]
	Female n=7 [n=20, 35.0%]	0 [n=7, 0.0%]	3 [n=7, 42.9%]	4 [n=7, 57.1%]
Age distribution	Minimum 20 years	39	20	40
	Maximum 81 years	64	59	81
	Median 47.5 years	42	37.5	61
Admitting condition	Trauma 7 [n=20, 35.0%]	3 [n=7, 42.9%]	4 [n=7, 57.1%]	0 [n=7, 0.0%]
	Medical 5 [n=20, 25.0%]	0 [n=5, 0.0%]	0 [n=5, 0.0%]	5 [n=5, 100%]
	Surgical 6 [n=20, 30.0%]	0 [n=6, 0.0%]	4 [n=6, 66.7%]	2 [n=6, 33.3%]
	Obstetric 0 [n=20, 0.0%]	0 [n=0, 0.0%]	0 [n=0, 0.0%]	0 [n=0, 0.0%]
	Cardiac surgery 2 [n=20, 10.0%]	0 [n=2, 0.0%]	0 [n=2, 0.0%]	2 [n=2, 100%]

Table 3.2 Inspection of carbapenem infusion labelling

	ICU A	ICU B	ICU C
Hospital n=3	Regional public hospital	Tertiary public hospital	Private hospital
General ICU n=3	Six bed closed ICU admitting adults and children over 12 years	15 bed closed ICU admitting adults	10 bed open ICU admitting all ages
Observations (n=223) of study patients (n=20) placed on carbapenem treatment	Twenty-nine (13.0%) observations of three patients prescribed Meropenem	Sixty-three (28.3%) observations of eight patients prescribed Imipenem	One hundred and thirty-one (58.7%) observations of nine patients prescribed Meropenem/ Ertapenem/ Doripenem
Inspection of carbapenem infusion bags labels (n=144)	Nineteen (29, 65.5%) infusion bags inspected	Forty-seven (63, 74.6%) infusion bags inspected	Seventy-eight (131, 59.5%) infusion bags inspected

Table 3.3 Documentation of dose administration in medication chart

Researcher observation n=223 [05h00-22h00]		Carbapenem dose administered at scheduled time [15min leeway accepted] 78 [n=223, 34.9%]	Documented time of administration correctly 61 [n=223, 27.4%]	Incorrect number of vials reconstituted – *documented that correct dose was given* 3 [n=223, 1.4%]	Missed carbapenem dose – *documented that dose was given* 12 [n=223, 5.4%]
Hospitals	Private hospital 131 [n=223, 58.7%]	48 [n=131, 36.6%]	35 [n=131, 26.7%]	2 [n=131, 1.5%]	5 [n=131, 3.8%]
	Public hospital 92 [n=223, 41.3%]	30 [n=92, 32.6%]	26 [n=92, 28.3%]	1 [n=92, 1.1%]	7 [n=92, 7.6%]
	p values	0.63	0.8	>0.999	0.24
Shifts day/night	Day shift 142 [n=223, 63.7%]	46 [n=142, 32.4%]	33 [n=142, 23.2%]	3 [n=142, 2.1%]	10 [n=142, 7.0%]
	Night shift 81 [n=223, 36.3%]	32 [n=81, 34.9%]	28 [n=81, 34.6%]	0 [n=81, 0.0%]	2 [n=81, 2.5%]
	p values	0.28	0.07	0.3	0.2
Shifts weekday	Weekday 143 [n=223, 64.1%]	53 [n=143, 37.1%]	39 [n=143, 27.3%]	1 [n=143, 0.7%]	10 [n=143, 7.0%]
	Weekend /Public holidays 80 [n=223, 35.9%]	25 [n=80, 31.3%]	22 [n=80, 27.5%]	2 [n=80, 2.5%]	2 [n=80, 2.5%]
	p values	0.38	>0.999	0.55	0.33
Qualifications	ICU-trained RN 38 [n=223, 17.0%]	16 [n=38, 42.1%]	13 [n=38, 34.2%]	1 [n=38, 2.6%]	0 [n=38, 0.0%]
	non-ICU trained RN 156 [n=223, 70.0%]	53 [n=156, 34.0%]	43 [n=156, 27.6%]	1 [n=156, 0.6%]	10 [n=156, 6.4%]
	EN 29 [n=223, 13.0%]	9 [n=29, 31.0%]	5 [n=29, 17.2%]	1 [n=29, 3.4%]	2 [n=29, 6.9%]
	p values	0.57	0.3	0.2	0.26
*Private healthcare sector only n=131	Hospital employed nurses* 98[n=131,74.8%]	41 [n=98, 41.8%]	28 [n=98, 28.6%]	2 [n=98, 2.0%]	2 [n=98, 2.0%]
	Agency nurses* 33 [n=131, 25.2%]	7 [n=33, 21.2%]	7 [n=33, 21.2%]	0 [n=33, 0.0%]	3 [n=33, 9.1%]
	p values	0.034	0.41	>0.999	0.1

Table 3.4 Medication information on carbapenem infusion bags

Pts [n=20]	Infusion bags sampled 144 [n=223, 64.6%]	Sticker label used to record information 75 [52.1%]	Permanent marker used to record information 38 [26.4%]	No information placed on infusion bag 31 [21.5%]	Patient name and number 49 [34.0%]	Medication name 110 [76.4%]	Medication dose 107 [74.3%]	Date 80 [55.6%]	Time 89 [61.8%]	Signature of RN mixing + administering dose* 27 [18.8%]	Signature of nurse checking dose** 33 [22.9%]
p values		<0.001	<0.001	0.45	<0.001	0.33	0.29	0.003	0.26	<0.001	<0.001
ICU A	19 [n=223, 8.5%]	15 [19, 78.9%] CI95: 54.4%-94.0%	2 [19, 10.5%] CI95: 1.3%-33.1%	2 [19, 10.5%] CI95: 1.3%-33.1%	0 [19, 0.0%] CI95: 0%-17.6%	17 [19, 89.5%] CI95: 66.9%-98.7%	17 [19, 89.5%] CI95: 66.9%-98.7%	14 [19, 73.7%] CI95: 48.8%-90.8%	14 [19, 73.7%] CI95: 48.8%-90.8%	14 [19, 73.7%] CI95: 48.8%-90.8%	9 [19, 47.4%] CI95: 24.4%-71.1%
ICU B	47 [n=223, 21.1%]	6 [47, 12.8%] CI95: 4.8%-25.7%	31 [47, 66.0%] CI95: 50.7%-79.1%	10 [47, 21.3%] CI95: 10.7%-35.7%	0 [47, 0.0%] CI95: 0%-7.5%	36 [47, 76.6%] CI95: 62.0%-87.7%	34 [47, 72.3%] CI95: 57.4%-84.4%	17 [47, 36.2%] CI95: 22.7%-51.5%	25 [47, 53.2%] CI95: 38.1%-67.9%	0 [47, 0.0%] CI95: 0%-7.5%	0 [47, 0.0%] CI95: 0%-7.5%
ICU C	78 [n=223, 35.0%]	54 [78, 69.2%] CI95: 57.8%-69.2%	5 [78, 6.4%] CI95: 2.1%-14.3%	19 [78, 24.4%] CI95: 15.3%-35.4%	49 [78, 62.8%] CI95: 51.1%-73.5%	57 [78, 73.1%] CI95: 61.8%-82.5%	56 [78, 71.8%] CI95: 60.5%-81.4%	49 [78, 62.8%] CI95: 51.1%-73.5%	50 [78, 64.1%] CI95: 52.4%-74.7%	13 [78, 16.7%] CI95: 9.2%-26.8%	24 [78, 30.8%] CI95: 20.8%-42.2%

Table 3.5 Essential information on carbapenem infusion bags

Carbapenem infusion bag sampled n=144		Medication details noted on carbapenem infusion bag 113 [n=144, 78.5%]	Essential information noted on carbapenem infusion bag* 12 [n=144, 8.3%]
Hospitals	Private hospital 78 [n=144, 54.2%]	59 [n=78, 75.6%]	12 [n=78, 15.4%]
	Public hospital 66 [n=144, 45.8%]	54 [n=66, 81.8%]	0 [n=66, 0.0%]
	p values	0.37	<0.001
Shifts day/ night	Day shift 73 [n=144, 50.7%]	55 [n=73, 75.3%]	6 [n=73, 8.2%]
	Night shift 71 [n=144, 49.3%]	58 [n=71, 81.7%]	6 [n=71, 8.4%]
	p values	0.35	>0.999
Shifts weekday	Weekday 91 [n=144, 63.2%]	72 [n=91, 79.1%]	8 [n=91, 8.8%]
	Weekend /Public holidays 53 [n=144, 36.8%]	41 [n-53, 77.4%]	4 [n=53, 7.5%]
	p values	0.8	>0.999
Qualifications	ICU-trained RN 24 [n=144, 16.7%]	19 [n=24, 79.2%]	1 [n=24, 4.2%]
	non-ICU trained RN 106 [n=144, 73.6%]	87 [n=106, 82.1%]	11 [n=106, 10.4%]
	EN 14 [n=144, 9.7%]	7 [n=14, 50.0%]	0 [n=14, 0.0%]
	p values	0.023	0.46
Private healthcare sector only	Hospital employed nurses 64 [n=78, 82.1%]	49 [n=64, 76.6%]	11 [n=64, 17.2%]
	Agency nurses 14 [n=78, 17.9%]	10 [n=14, 71.4%]	1 [n=14, 7.1%]
	p values	0.74	0.45

*Essential information: Patient's name, drug, dose, date, time, signature of nurse mixing and administering dose

Table 3.6 Compliance with dose timing and infusion duration

Researcher observation n=223 [05h00-22h00]		Carbapenem dose administered early 64 [n=223, 28.7%]	Carbapenem dose administered late 69 [n=223, 30.9%]	Compliant with duration instructions* 117 [n=195, 60.0%]
Hospitals	Private hospital 131 [n=223, 58.7%]	43 [n=131, 32.8%]	34 [n=131, 26.0%]	72 [n=112, 64.3%]
	Public hospital 92 [n=223, 41.3%]	21 [n=92, 22.8%]	35 [n=92, 38.0%]	45 [n=83, 54.2%]
	p values	0.1	0.055	0.16
Shifts day/night	Day shift 142 [n=223, 63.7%]	32 [n=142, 22.5%]	54 [n=142, 38.0%]	72 [n=127, 56.7%]
	Night shift 81 [n=223, 36.3%]	32 [n=81, 39.5%]	15 [n=81, 18.5%]	45 [n=68, 66.2%]
	p values	0.007	0.024	0.197
Shifts weekday	Weekday 143 [n=223, 64.1%]	41 [n=143, 28.7%]	39 [n=143, 27.3%]	73 [n=122, 59.8%]
	Weekend /Public holidays 80 [n=223, 35.9%]	23 [n=80, 28.8%]	30 [n=80, 37.5%]	44 [n=73, 60.3%]
	p values	1.0	0.11	1.0
Qualifications	ICU trained RN 38 [n=223, 17.0%]	9 [n=38, 23.7%]	13 [n=38, 34.2%]	23 [n=36, 63.9%]
	non-ICU trained RN 156 [n=223, 70.0%]	46 [n=156, 29.5%]	47 [n=156, 30.1%]	80 [n=136, 58.8%]
	EN 29 [n=223, 13.0%]	9 [n=29, 31.0%]	9 [n=29, 31.0%]	14 [n=23, 60.9%]
	p values	0.84	0.88	0.86
*Private healthcare sector only n=131	Hospital employed nurses* 98 [n=131, 74.8%]	29 [n=98, 29.6%]	26 [n=98, 26.5%]	54 [n=86, 62.8%]
	Agency nurses* 33 [n=131, 25.2%]	14 [n=33, 42.4%]	9 [n=33, 27.3%]	18 [n=26, 69.2%]
	p values	0.17	0.92	0.55

*Completion time not observed in 28 doses

Table 3.7 Volumetric analysis of residual carbapenem in used (discarded) items [%]

Volumetric analysis % drug in discarded items	Items analysed	Min %	Max %	Median %	Mean %	Std Dev	IQR %	p values
Carbapenem vials	137 (n=223, 61.4%)	0.0	26.0	3.6	4.9	4.4	2.0-6.9	
Syringes used to reconstitute dose	94 (n=223, 42.2%)	0.0	11.1	0.65	1.2	1.9	0.0-1.4	
Infusion bags	122 (n=223, 64.6%)	0.0	60.0	3.6	7.5	9.5	0.7-10.3	< 0.001
Infusion lines [volumetric, gravity feed, secondary]	73 (n=223, 32.7%)	9.5	76.0	28.2	30.8	15.1	24.7-48.5	

Table 3.8 Percentage antibiotic loss in infusion items retrieved at same dose administrations

Items retrieved at same dose administrations	Doses	Min %	Max %	Mean %	Std Deviation	p value
4 items [all items retrieved: vial, syringe, infusion bag, and infusion line]	17	14.5	88.0	50.0	20.3	
2 items *Preparation phase* [vial, and syringe retrieved]	93	0.0	28.0	7.1	5.8	<0.001
2 items *Administration phase* [bag and line retrieved]	37	9.5	100	40.1	18.8	

Table 3.9 Observed syringe choice with percentage of dose inserted into bag

Volumetric analysis	Syringes and bags 134 [n=158, 86.7%]	Min %	Max %	Median %	Mean %	Std Deviation %
20 ml syringe	11 [n=134, 8.2%]	92.5	99.0	97.9	97.2	2.0
10 ml syringe	83 [n=134, 61.9%]	82.8	100	97.0	96.6	2.6
5, 3, 2.5ml syringes	40 [n=134, 29.9%]	72.0	96.0	89.8	88.6	5.4

Table 3.10 Antibiotic residue found in discarded items during preparation phase

Retrieved items at carbapenem administrations n=223		Carbapenem residual volume in discarded vial 135 [n=137, 98.5%]	Carbapenem residual volume in discarded syringe 70 [n=94, 74.5%]	Incomplete dose inserted into infusion bag 135 [n=137, 98.5%]	Missed carbapenem doses observed 12 [n=223, 5.4%]	Incorrect dose given [incorrect number of vials reconstituted] 3 [n=223, 1.4%]
Items sampled		137 vials sampled [n=223, 61.4%]	94 syringes sampled [n=223, 42.2%]	137 bags calculated [n=223, 61.4%]	12 doses not given [n=223, 5.4%]	3 doses used incorrect number of vials [n=223, 1.4%]
Hospitals	Private hospital 123 [n=223, 55.2%]	86 [n=86, 100%]	42 [n=51, 82.4%]	86 [n=86, 100%]	5 [n=123, 4.1%]	2 [n=123, 1.6%]
	Public hospital 100 [n=223, 44.8%]	49 [n=51, 96.1%]	28 [n=43, 65.1%]	49 [n=51, 96.1%]	7 [n=100, 7.0%]	1 [n=100, 1.0%]
	p values	0.14	0.056	0.14	0.33	1.0
Shifts day/night	Day shift 122 [n=223, 54.7%]	82 [n=84, 97.6%]	39 [n=58, 67.2%]	82 [n=84, 97.6%]	10 [n=122, 8.2%]	3 [n=122, 2.5%]
	Night shift 101 [n=223, 45.3%]	53 [n=53, 100%]	31 [n=36, 86.1%]	53 [n=53, 100%]	2 [n=101, 2.0%]	0 [n=101, 0.0%]
	p values	0.52	0.041	0.52	0.041	0.25
Shifts Weekday	Weekday 146 [n=223, 65.5%]	83 [n=84, 98.8%]	44 [n=60, 73.3%]	83 [n=84, 98.8%]	10 [n=146, 6.8%]	1 [n=146, 0.7%]
	Weekend /Public holidays 77 [n=223, 34.5%]	52 [n=53, 98.1%]	26 [n=34, 76.5%]	52 [n=53, 98.1%]	2 [n=77, 2.6%]	2 [n=77, 2.6%]
	p values	1.0	0.74	1.0	0.23	0.55
Qualifications	ICU trained RN 33 [n=223, 14.8%]	20 [n=22, 90.9%]	13 [n=18, 72.2%]	20 [n=22, 90.9%]	0 [n=33, 0.0%]	1 [n=33, 3.0%]
	non-ICU trained RN 160 [n=223, 71.7%]	98 [n=98, 100%]	51 [n=69, 73.9%]	98 [n=98, 100%]	10 [n=160, 6.3%]	1 [n=160, 0.6%]
	EN 30 [n=223, 13.5%]	17 [n=17, 100%]	6 [n=7, 85.7%]	17 [n=17, 100%]	2 [n=30, 6.7%]	1 [n=30, 3.3%]
	p values	0.039	0.85	0.039	0.322	0.193
*Private healthcare sector only n=123	Hospital employed nurses* 89 [n=123, 72.4%]	69 [n=69, 100%]	33 [n=41, 80.5%]	69 [n=69, 100%]	2 [n=89, 2.2%]	2 [n=89, 2.2%]
	Agency nurses* 34 [n=123, 27.6%]	17 [n=17, 100%]	9 [n=10, 90.0%]	17 [n=17, 100%]	3 [n=34, 8.8%]	0 [n=36, 0.0%]
	p values	n/a	0.67	n/a	0.13	1.0

Table 3.11 Antibiotic residue found in discarded items during administration phase

Retrieved items at carbapenem administrations n=223		Carbapenem residual volume in discarded infusion bags 122 [n=144, 84.7%]	Carbapenem residual volume in discarded volumetric administration sets 47 [n=47, 100%]	Carbapenem residual volume in discarded gravity administration sets 4 [n=4, 100%]	Carbapenem residual volume in discarded 'add on line' administration sets 31 [n=31, 100%]
Items sampled		144 infusion bags sampled [n=223, 64.7%]	47 administration sets sampled [n=223, 21.1%]	4 administration sets sampled [n=223, 1.8%]	31 administration sets sampled [n=223, 13.9%]
Hospitals	Private hospital 123 [n=223, 55.2%]	66 [n=78, 84.6%]	19 [n=19, 100%]	n/a	31 [n=31, 100%]
	Public hospital 100 [n=223, 44.8%]	56 [n=66, 84.8%]	28 [n=28, 100%]	4 [n=4, 100%]	n/a
	p values	0.9	n/a	n/a	n/a
Shifts day/night	Day shift 122 [n=223, 54.7%]	63 [n=73, 87.7%]	31 [n=31, 100%]	1 [n=1, 100%]	12 [n=12, 100%]
	Night shift 101 [n=223, 45.3%]	59 [n= 71, 83.1%]	16 [n=16, 100%]	3 [n=3, 100%]	19 [n=19, 100%]
	p values	0.59	n/a	n/a	n/a
Shifts Weekday	Weekday 146 [n=223, 65.5%]	76 [n= 91, 83.5%]	32 [n=32, 100%]	4 [n=4, 100%]	20 [n=20, 100%]
	Weekend /Public holidays 77 [n=223, 34.5%]	46 [n=53, 86.3%]	15 [n=15, 100%]	0 [n=0, 100%]	11 [n=31, 100%]
	p values	0.60	n/a	n/a	n/a
Qualifications	ICU trained RN 33 [n=223, 14.8%]	20 [n=24, 83.3%]	10 [n=10, 100%]	1 [n=1, 100%]	n/a
	non-ICU trained RN 160 [n=223, 71.7%]	92 [n=106, 86.8%]	35 [n=35, 100%]	3 [n=3, 100%]	21 [n=21, 100%]
	EN 30 [n=223, 13.5%]	10 [n=14, 71.4%]	2 [n=2, 100%]	n/a	10 [n=10, 100%]
	p values	0.316	n/a	n/a	n/a
*Private healthcare sector only n=123	Hospital employed nurses* 89 [n=123, 72.4%]	57 [n=64, 89.1%]	16 [n=16, 100%]	n/a	19 [n=19, 100%]
	Agency nurses* 34 [n=123, 27.6%]	9 [n=14, 64.3%]	3 [n=3, 100%]	n/a	12 [n=12, 100%]
	p values	0.034	n/a	n/a	n/a

Table 3.12 Patient demographics

Patients 20 [n=105, 19%]	A 2	A 30	A 31	B 4	B 7	B 10	B 11	B 14	B 19	B 44	B 52	C 4	C 5	C 6	C 8	C 11	C 12	C 13	C 15	C 22
Gender M 13 [65.0%] F 7 [35.0%]	M	M	M	M	F	F	F	M	M	M	M	F	M	M	M	M	F	F	F	M
Age Mean 50.15 SD 16.31685	64	39	42	37	20	53	37	59	50	21	38	71	81	68	61	52	64	43	40	63
Condition	Trauma	Trauma	Trauma	Surgical	Trauma	Surgical	Surgical	Trauma	Surgical	Trauma	Trauma	Surgical	Medical	Medical	Medical	Cardiac surgery	Medical	Cardiac surgery	Medical	Surgical
	Lap blunt abdominal trauma [mauled by a	TBI, crush injury [community assault]	Polytrauma [motor vehicle collision]	Relap acute abdomen [bowel perforation]	Relap gunshot abdomen	Relap perforated small bowel [8 previous laps]	Lap intra-abdominal bleed [molar	Relap gunshot abdomen	Closure complicated diaphramatic hernia	Polytrauma [motor vehicle collision]	Lap gunshot abdomen	Lap small bowel obstruction	Hypertension urgency	CVA [basal ganglia]	Status epilepticus	Coronary Artery Bypass Graft x 3	Congestive cardiac failure	Mitral valve replacement	Hypoxic pneumonia Congestive cardiac	Lap cholecystectomy
Carbapenem prescription	Meropenem 1g 8hrly over 3 hours*	Meropenem 2g 8hrly over 3 hours*	Meropenem 2g 8hrly over 3 hours*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Imipenem 1g 6hrly over 1 hour*	Meropenem 2g 8hrly over 3 hours#	Ertapenem 1g daily over 30 min**	Meropenem 1g 8hrly over 15-30m**	Ertapenem 1g daily over 30 min**	Meropenem 1g 8hrly over 15-30m**	Meropenem 1g 1st and 2nd course Meropenem 500mg 3rd course over 15-30m**	Meropenem 1g 8hrly over 15-30m**	Doripenem 500mg 8hrly over 1h**	Meropenem 1g 8hrly over 15-30m**

Table 3.13 Drug loss to study patients (percentage), rectal swab isolates and mc&s results, timing (days following carbapenem initiation), length of ICU stay (days) and mortality

Pts n=20	Carbapenem Rx AB doses while in ICU n=389	Total number of doses analysed n=223	mean (sd) % drug lost per dose	Rectal swab CRE isolated [dose of carbapenem rx]	mc+s carbapenem resistance [day of carbapenem rx]	mc+s MDRO [day of carbapenem rx]	LOS*	Death
A2	12	10	19.8 (20.5) %	Day 5, dose 12	Day 4	-	8	-
A30	25	12	24.0 (25.0) %	CRE isolated before rx commenced	Day 5	Day 5	31	-
A31	16	5	25.5 (24.5) %	-	-	Before rx	18	-
B4	24	6	53.6 (36.0) %	-	-	Before rx	8	-
B7	4	1	100%	-	-	Before rx	4	-
B10	7	3	15.5 (8.0) %	-	-	Before rx	2	-
B11	10	4	14.5 (7.5) %	-	-	-	4	-
B14	17	5	18.1 (8.9) %	-	-	-	6	-
B19	22	10	27.2 (29.1) %	-	Day 6	Day 4	14	-
B44	56	34	19.6 (23.2) %	-	Day 2	Before rx	32	-
B52	21	10	34.9 (37.7) %	-	Day 5	-	10	Died
C4	20	13	25.0 (23.5) %	CRE isolated before rx commenced	Unknown, no mc+s taken	Unknown, no mc+s taken	9	Died
C5	4	3	23.0 (24.7) %	-	Unknown, no mc+s taken	Unknown, no mc+s taken	10	-
C6	18	9	26.1 (25.5) %	-	Unknown, no mc+s taken	Unknown, no mc+s taken	11	-
C8	32 [+2 doses prior to admission to ICU]	29	23.6 (25.9) %	-	Unknown, no mc+s taken	Unknown, no mc+s taken	15	-
C11	5	5	33.5 (38.7) %	-	-	-	5	-
C12	59 [+25 doses prior to admission to ICU]	38	17.9 (19.5) %	Day 10, dose 25	Day 25	Day 15	64	Died
C13	14	10	26.0 (19.7) %	-	Unknown, no mc+s taken	Unknown, no mc+s taken	12	-
C15	16 [+4 doses prior to admission to ICU]	12	48.0 (40.2) %	Day 14, dose 20	Day 17	-	25	-
C22	7 [+9 doses prior to admission to ICU]	4	6.4 (5.1) %	Day 10, dose 15	Unknown, no mc+s taken	Unknown, no mc+s taken	4	-

Table 3.14 Study patients and carbapenem administration errors

Patients n=20			A 2	A 30	A 31	B 4	B 7	B 10	B 11	B 14	B 19	B 44	B 52	C 4	C 5	C 6	C 8	C 11	C 12	C 13	C 15	C 22
223 doses observed	Sampling n=1813	Errors 950 [52.4%]	31 64	62 130	21 42	32 50	5 8	7 18	13 26	14 43	30 57	150 239	52 78	60 109	14 25	42 79	146 248	20 37	134 349	48 96	55 87	14 28
Missed dose errors	223 administrations	12 [n=223, 5.4%]	0 8	0 16	0 5	2 7	0 1	0 2	0 3	0 5	1 7	2 28	2 10	0 13	0 3	0 11	1 31	1 5	0 42	0 12	3 11	0 3
Incorrect number of vial errors	223 administrations	3 [n=223, 1.4%]	0 8	0 16	0 5	0 7	0 1	0 2	0 3	0 5	0 7	0 28	1 10	2 13	0 3	0 11	0 31	0 5	0 42	0 12	0 11	0 3
Reconstitution errors	178 diluent volumes	95 [n=178, 53.4%]	3 5	10 14	3 5	4 5	n/a	2 2	2 2	4 5	1 6	8 22	6 8	6 10	0 3	2 7	13 23	2 3	16 37	5 11	6 7	2 3
Labelling errors	144 infusion bags	132 [n=144, 91.7%]	5 5	11 11	3 3	2 2	1 1	2 2	4 4	3 3	6 6	25 25	4 4	8 8	1 1	2 3	18 20	2 2	20 26	5 5	6 9	4 4
Time errors	223 administrations	145 [n=223, 65.0%]	3 8	9 16	3 5	6 7	1 1	0 2	1 3	0 5	5 7	26 28	8 10	7 13	3 3	10 11	26 31	4 5	15 42	9 12	8 11	1 3
Dose interval errors	223 administrations	145 [n=223, 65.0%]	3 8	9 16	3 5	6 7	1 1	0 2	1 3	0 5	5 7	26 28	8 10	7 13	3 3	10 11	26 31	4 5	15 42	9 12	8 11	1 3
Signing off errors	223 medication charts	162 [n=223, 72.6%]	6 8	9 16	3 5	6 7	1 1	0 2	2 3	1 5	5 7	26 28	7 10	10 13	3 3	10 11	25 31	4 5	23 42	9 12	10 11	2 3
Duration errors	195 administrations	78 [n=195, 40.0%]	4 7	5 16	2 5	3 5	0 1	1 2	1 3	1 5	2 5	11 26	8 8	7 13	1 3	1 7	10 23	0 4	12 41	2 10	6 8	1 3
Flushing errors	181 administrations	178 [n=181, 98.3%]	7 7	9 9	4 4	3 3	1 1	2 2	2 2	5 5	5 5	26 26	8 8	13 13	3 3	7 7	27 27	3 3	33 35	9 10	8 8	3 3
223 doses analysed	Sampling n=457	Errors 409 [89.5%]	10 18	34 35	9 10	10 10	2 2	6 7	8 8	10 11	10 12	51 62	15 17	19 23	6 6	18 18	57 62	7 9	86 89	22 24	21 25	8 9
Loss of dose in vial	137 vials	135 [n=137, 98.5%]	3 5	10 10	3 3	2 2	n/a	2 2	2 2	3 3	1 1	17 17	6 6	7 7	2 2	5 5	17 17	3 3	33 33	9 9	7 7	3 3
Loss of dose in syringe	94 syringes	70 [n=94, 74.5%]	1 5	9 10	2 2	2 2	n/a	1 2	2 2	2 3	1 1	3 11	5 5	2 2	2 2	4 4	8 10	2 2	15 18	4 6	4 5	1 2
Loss of dose in infusion bag	144 infusion bags	122 [n=144, 84.7%]	3 5	11 11	2 3	2 2	1 1	2 2	4 4	3 3	4 6	22 25	2 4	4 8	1 1	3 3	17 20	0 2	26 26	5 5	6 9	4 4
Loss of dose in infusion line	82 infusion lines	82 [n=82, 100%]	3 3	4 4	2 2	4 4	1 1	1 1	n/a	2 2	4 4	9 9	2 2	6 6	1 1	6 6	15 15	2 2	12 12	4 4	4 4	n/a

Table 3.15 Infusion errors observed

223 doses observed			Hospitals		Shifts		Day		Qualifications			Private only	
			Public 92 [n=223, 41.3%]	Private 131 [n=223, 58.7%]	Day 142 [n=223, 63.7%]	Night 81 [n=223, 36.3%]	Week day 143 [n=223, 64.1%]	Week-end + PH 80 [n=223, 35.9%]	ICU trained RN 38 [n=223, 17.0%]	RN 156 [n=223, 70.0%]	EN 29 [n=223, 13.0%]	Hospital employed 98 [n=131, 74.8%]	Agency 33 [n=131, 25.2%]
	Sampling n=1813	Errors 950 [52.4%]	417 [n=950, 43.9%]	533 [n=950, 56.1%]	624 [n=950, 65.7%]	326 [n=950, 34.3%]	599 [n=950, 63.1%]	351 [n=950, 36.9%]	151 [n=950, 15.9%]	672 [n=950, 70.7%]	127 [n=950, 13.4%]	396 [n=533, 74.3%]	137 [n=533, 25.7%]
Missed dose errors	223 administrations	12 [n=223, 5.4%]	7 [n=92, 7.6%]	5 [n=131, 3.8%]	10 [n=142, 7.0%]	2 [n=81, 2.5%]	10 [n=143, 7.0%]	2 [n=80, 2.5%]	0 [n=38, 0.0%]	10 [n=156, 6.4%]	2 [n=29, 6.9%]	2 [n=98, 2.0%]	3 [n=33, 9.1%]
P values			0.24		0.2		0.33		0.26			0.1	
Incorrect number of vial errors	223 administrations	3 [n=223, 1.4%]	1 [n=92, 1.1%]	2 [n=131, 1.5%]	3 [n=142, 2.1%]	0 [n=81, 0.0%]	1 [n=143, 0.7%]	2 [n=80, 2.5%]	1 [n=38, 2.6%]	1 [n=156, 0.6%]	1 [n=29, 3.4%]	2 [n=98, 2.0%]	0 [n=33, 0.0%]
P values			1.0		0.3		0.55		0.2			1.0	
Reconstitution errors	178 diluent volumes	95 [n=178, 53.4%]	43 [n=74, 58.1%]	52 [n=104, 50.0%]	64 [n=116, 55.2%]	31 [n=62, 50.0%]	60 [n=111, 54.1%]	35 [n=67, 52.2%]	17 [n=31, 54.8%]	66 [n=115, 57.4%]	12 [n=22, 54.5%]	40 [n=81, 49.4%]	12 [n=23, 52.2%]
P values			0.35		0.049		0.89		0.85			0.9	
Labelling errors	144 infusion bags	132 [n=144, 91.7%]	66 [n=66, 100%]	66 [n=78, 84.6%]	67 [n=73, 91.8%]	65 [n=71, 91.5%]	83 [n=91, 91.2%]	49 [n=53, 92.5%]	23 [n=24, 95.8%]	95 [n=106, 89.6%]	14 [n=14, 100%]	53 [n=64, 82.8%]	13 [n=14, 92.9%]
P values			0.001		1.0		1.0		0.46			0.45	
Time errors	223 administrations	145 [n=223, 65.0%]	62 [n=92, 67.4%]	83 [n=131, 63.4%]	96 [n=142, 67.6%]	49 [n=81, 60.5%]	90 [n=143, 62.9%]	55 [n=80, 68.8%]	22 [n=38, 57.9%]	103 [n=156, 66.0%]	20 [n=29, 69.0%]	57 [n=98, 58.2%]	26 [n=33, 78.8%]
P values			0.5		0.22		0.34		0.59			0.034	
Dose interval errors	223 administrations	145 [n=223, 65.0%]	62 [n=92, 67.4%]	83 [n=131, 63.4%]	96 [n=142, 67.6%]	49 [n=81, 60.5%]	90 [n=143, 62.9%]	55 [n=80, 68.8%]	22 [n=38, 57.9%]	103 [n=156, 66.0%]	20 [n=29, 69.0%]	57 [n=98, 58.2%]	26 [n=33, 78.8%]
P values			0.5		0.22		0.34		0.59			0.034	

Signing off errors	223 medication charts	162 [n=223, 72.6%]	66 [n=92, 71.7%]	96 [n=131, 73.3%]	109 [n=142, 76.8%]	53 [n=81, 65.4%]	104 [n=143, 72.7%]	58 [n=80, 72.5%]	25 [n=38, 65.8%]	113 [n-156, 72.4%]	24 [n=29, 82.8%]	70 [n=98, 71.4%]	26 [n=33, 78.8%]
P values			0.81		0.07		1.0		0.3			0.41	
Duration errors	195 administrations	78 [n=195, 40.0%]	38 [n=83, 45.8%]	40 [n=112, 35.7%]	55 [n=127, 43.3%]	23 [n=68, 33.8%]	49 [n=122, 40.2%]	29 [n=73, 39.7%]	13 [n=36, 36.1%]	56 [n=136, 41.2%]	9 [n=23, 39.1%]	32 [n=86, 37.2%]	8 [n=26, 30.8%]
P values			0.16		0.197		1.0		0.86			0.55	
Flushing errors	181 administrations	178 [n=181, 98.3%]	72 [n=72, 100%]	106 [n=109, 97.2%]	124 [n=126, 98.4%]	54 [n=55, 98.2%]	112 [n=115, 97.4%]	66 [n=66, 100%]	28 [n=28, 100%]	125 [n=128, 97.7%]	25 [n=25, 100%]	83 [n=84, 98.8%]	23 [n=25, 92.0%]
P values			0.28		1.0		0.3		1.0			0.13	

Table 3.16 Infusion errors measured from used and discarded infusion items (vials, syringes, infusion bags, infusion lines)

223 doses analysed			Public 100 [n=223, 44.8%]	Private 123 [n=223, 55.2%]	Day 122 [n=223,54.7%]	Night 101 [n=223, 45.3%]	Week Day 146 [n=223, 65.5%]	Week-end + PH 77 [n=223, 34.5%]	ICU trained RN 33 [n=223, 14.8%]	RN 160 [n=223, 71.7%]	EN 30 [n=223, 13.5%]	Hospital employed 89 [n=123, 72.4%]	Agency 34 [n=123, 27.6%]
	Sampling n=457	Errors 409 [89.5 %]	165 [n=409, 40.3%]	244 [n=409, 59.7%]	228 [n=409, 55.7%]	181 [n=409, 44.3%]	259 [n=409, 63.3%]	150 [n=409, 36.7%]	64 [n=409, 15.6%]	300 [n=409, 73.3%]	45 [n=409, 11.0%]	194 [n=244, 79.5%]	50 [n=244, 20.5%]
Loss of dose in vial	137 vials	135 [n=137, 98.5%]	49 [n=51, 96.1%]	86 [n=86, 100%]	82 [n=84, 97.6%]	53 [n=53, 100%]	83 [n=84, 98.8%]	52 [n=53, 98.1%]	20 [n=22, 90.9%]	98 [n=98, 100%]	17 [n=17, 100%]	69 [n=69 100%]	17 [n=17 100%]
P values			0.14		0.52		1.0		0.039			n/a	
Loss of dose in syringe	94 syringes	70 [n=94, 74.5%]	28 [n=43, 65.1%]	42 [n=51, 82.4%]	39 [n=58, 67.2%]	31 [n=36 86.1%]	44 [n=60, 73.3%]	26 [n=34 76.5%]	13 [n=18, 72.2%]	51 [n=69, 73.9%]	6 [n=7 85.7%]	33 [n=41, 80.5%]	9 [n=10, 90.0%]
P values			0.056		0.041		0.74		0.85			0.67	
Loss of dose in infusion bag	144 infusion bags	122 [n=144, 84.7%]	56 [n=66, 84.8%]	66 [n=78, 84.6%]	63 [n=73, 86.3%]	59 [n=71, 83.1%]	76 [n=91, 83.5%]	46 [n=53, 86.8%]	20 [n=24, 83.3%]	92 [n=106, 86.8%]	10 [n=14, 71.4%]	57 [n=64, 89.1%]	9 [n=14 64.3%]
P values			0.9		0.59		0.60		0.316			0.034	
Loss of dose in infusion line	82 infusion lines	82 [n=82, 100%]	32 [n=32, 100%]	50 [n=50, 100%]	44 [n=44, 100%]	38 [n=38, 100%]	56 [n=56 100%]	26 [n=26, 100%]	11 [n=11, 100%]	59 [n=59, 100%]	12 [n=12, 100%]	35 [n=35, 100%]	15 [n=15, 100%]
P values			n/a		n/a		n/a		n/a			n/a	

Table 3.17 Example of antibiotic loss to patients at same dose administration [n=17]

Patient	Total number of doses received in study ICU	Total number of doses where all infusion items were retrieved and measured	Mean % drug lost per dose	Rectal swab CRE isolated [day of carbapenem rx]	mc+s carbapenem resistance [day of carbapenem rx]	mc+s MDRO [day of carbapenem rx]	LOS*	Death
A30	25	3	52.7%	Before rx commenced	Day 5	Day 5	31	Survived to discharge from ICU
B4	24	1	31.6%	-	-	Before rx	8	Survived to discharge from ICU
B44	56	3	28.5%	-	Day 2	Before rx	32	Survived to discharge from ICU
C6	18	1	64.7%	-	Unknown, no mc+s taken	Unknown, no mc+s taken	11	Survived to discharge from ICU
C8	34	3	40.9%	-	Unknown, no mc+s taken	Unknown, no mc+s taken	15	Survived to discharge from ICU
C12	59	3	50.4%	Day 10	Day 25	Day 15	64	Died
C13	14	1	40.6%	-	Unknown, no mc+s taken	Unknown, no mc+s taken	12	Survived to discharge from ICU
C15	20	2	74.5%	Day 14	Day 17	-	25	Survived to discharge from ICU

*Length of stay [days]