

Quality Evaluation of Clinical Pharmacy Services in an Intensive Care Unit

*A thesis submitted in partial fulfilment of the requirements of
the Degree of Doctorate in Pharmacy*

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To my family

Michael, Daniel, Matthea and Paula Marie

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Abstract

Due to complex pharmacotherapy often involving high-risk medications, critically ill patients are more vulnerable to adverse drug events. Pharmacists' participation in Intensive Care Units (ICUs) has been shown to improve patient outcomes, and it is important to ensure that the service provided is of quality and is effective to actually achieve these outcomes. This study aims to develop and implement a quality system for pharmaceutical service provision within the ICU and evaluate the activities of clinical pharmacists in intensive care by assessing the impact of pharmaceutical interventions on surrogate clinical outcomes.

The first phase of the study included consideration of current practices within the ICU to propose a hospital policy based on the Pharmacists' Patient Care Process to provide a structured framework and standardise the provision of clinical pharmacy services in the ICU. The policy was reviewed by an expert panel through a multi-level approach. During the second phase, a data collection tool was developed and validated to capture and classify drug-related problems (DRPs) and pharmaceutical interventions (PIs) suggested by pharmacists in the ICU. Data on PIs recommended by a team of clinical pharmacists over three months were recorded in the data collection tool and categorised. PIs were classified according to their impact on surrogate patient outcomes and retrospectively evaluated by an expert panel to assess the probability of a potential adverse drug event (ADE) occurring in the absence of the PI.

The developed policy includes responsibilities and comprises 11 main practices of the ICU pharmacy team related to direct patient care and indirect patient care. Over three

months, the ICU pharmacist-patient profiles of 164 patients were considered, where 484 DRPs were identified in 135 patients; 38% (n=186) were related to dose selection, 24% (n=115) involved drug selection, and 13% (n=65) were related to monitoring. Most suggested PIs were related to change in dose 40% (n=193) and addition of medication 17% (n=80). Anti-infectives for systemic use were the most common group of medications identified in DRPs (41%). Pharmacists assisted in optimising fluid management for 17 patients, which involved hidden fluids. Therapeutic drug monitoring was recommended for 43 patients with subsequent dose adjustments to achieve therapeutic serum concentrations for medications with a narrow therapeutic range. Expert panel evaluation of PIs in relation to preventing a potential ADE resulted in 5 (1%) being of high probability, 124 (25.6%) being of medium probability, and 274 (56.6%) being of low probability. The remaining 81 (16.7%) had a very low or zero probability of preventing a potential ADE.

This study aids in standardising clinical pharmacists' participation in the ICU and harmonises the quality of services. The study has indicated that pharmacists' interventions in the ICU are effective in reducing the risk of occurrence of potential ADEs. Whilst the risk impact was estimated to range between high to very low, a key aspect of patient-centric care is providing optimised pharmacotherapy to mitigate individual patient risks as a result of medication use.

Keywords: policy, pharmaceutical interventions, intensive care unit, drug-related problems, adverse drug events, patient outcomes

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List of abbreviations

ACCP	American College of Clinical Pharmacists
ADE	Adverse drug event
AF	Atrial fibrillation
AKI	Acute kidney injury
ATC	Anatomical therapeutic chemical
DRP	Drug-related problem
ESICM	European Society of Intensive Care Medicine
FICM	Faculty of Intensive Care Medicine
ICS	Intensive Care Society
ICU	Intensive Care Unit
IV	Intravenous
JCPP	Joint Commission of Pharmacy Practitioners
MDH	Mater Dei Hospital
OTC	Over-the-counter
pADE	Potential adverse drug event
PCNE	Pharmaceutical Care Network Europe
PI	Pharmaceutical intervention
SHPA	Society of Hospital Pharmacists of Australia
SLED	Sustained low-efficiency dialysis
SOP	Standard operating procedure
TDM	Therapeutic drug monitoring

Chapter 1
Introduction

1.1 Challenges of intensive care

Patients admitted to the Intensive Care Unit (ICU) pose distinct challenges to pharmacotherapy. These challenges arise from the severity of the illness and the complex medication requirements. Critical illness leads to substantial changes in drug pharmacokinetics and pharmacodynamics due to altered physiology and organ dysfunction, which may affect drug distribution, metabolism, and elimination (Hanks et al, 2022). Furthermore, organ support mechanisms, such as renal replacement therapies, also influence drug pharmacokinetics (Hanks et al, 2022). Critically ill patients also present with underlying health conditions which further affect medication choice or response. Additionally, ICU patients receive a high number of concurrent treatments and are generally prescribed twice the number of medications when compared to patients in other hospital wards (Richter et al, 2016).

In the ICU, patients are more vulnerable to adverse drug events (ADEs) than patients who do not require intensive care therapy (Kane-Gill et al, 2010). Critically ill patients are sicker than other patients, and due to the ICU environment, which is a high-risk setting, rapid changes in clinical conditions, high-alert medications administered intravenously, complex medication regimens and complex disease, they are at higher risk for ADEs, both potential ADEs and preventable ADEs (Kane-Gill et al, 2010). Compared to non-ICU settings, preventable ADEs are twice as probable to happen in ICUs, and they are more likely to result in life-threatening outcomes (Michalets et al, 2015).

1.2 Adverse Drug Events

An ADE can be defined as ‘any injury due to a medication’ (Bates et al 1995; Gandhi et al, 2000). Potential ADEs are events in which an incident occurred with a potential for injury (Gandhi et al, 2000). These include medication errors that are identified and intercepted by a healthcare provider or the patient before they actually reach the patient. Potential ADEs are also called ‘near-miss errors or close calls’¹. Preventable ADEs are those ADEs that result from medication errors that can be avoided¹. The relationship between ADEs, preventable ADEs, potential ADEs, and medication errors is described in Figure 1.1.

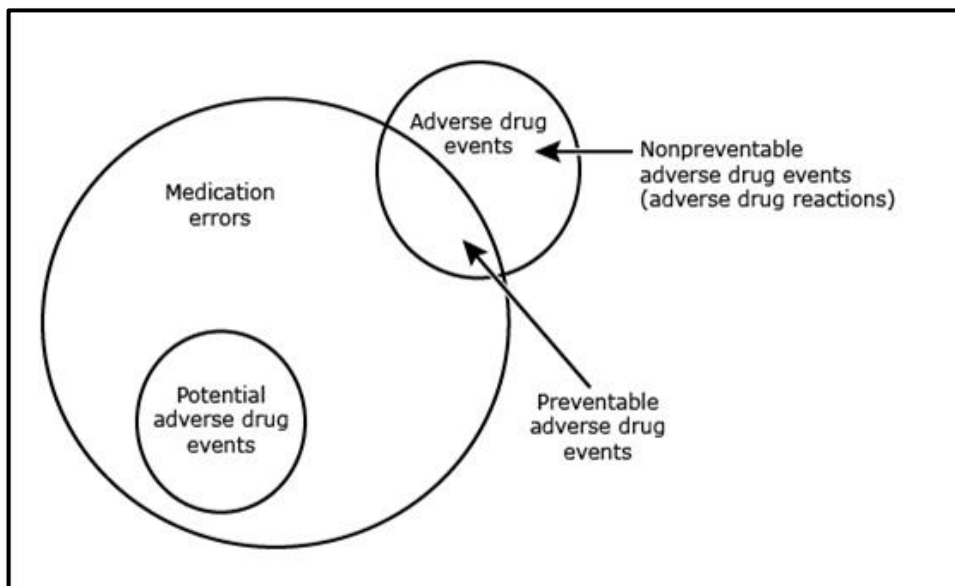


Figure 1.1: Relationship between medication errors, potential ADEs, preventable ADEs and ADEs. Reproduced from: Gandhi et al, 2000; Zhu and Weingart, 2024¹.

¹ Zhu J and Weingard SN. Prevention of Adverse Drug Events in Hospital. In: UpToDate, Auerbach AD and Givens J (Eds), UpToDate, Waltham, MA. (Accessed on April 28, 2024). Available from: <https://www.uptodate.com/contents/prevention-of-adverse-drug-events-in-hospitals>

Potential ADEs also encompass discrepancies in medication regimens, which may include omission of a medication or patient non-adherence, both of which carry a risk of patient harm (Kripalani et al, 2012; Mueller et al, 2012). A randomised controlled trial by Kripalani et al (2012) found that medication omissions and premature discontinuation of medications after hospital discharge can cause significant potential consequences and have been described as potential ADEs. Pharmacist interventions related to medication omissions were found to have at least a low probability of preventing an ADE in hospital patients, while in the ICU, omissions of medications during the transfer of patients were found to have a potential for patient harm (Gallagher et al, 2014; Bosma et al, 2018b).

1.3 Pharmacists in the intensive care unit

Given the complicated medication regimens of critical care patients, the pharmacist's role in the ICU has developed significantly and comprises working as a member of the interdisciplinary team providing a range of clinical services (Papadopoulos et al, 2002). In the United States, pharmacists were introduced in critical care decades ago, followed by the United Kingdom (Hunfeld et al, 2024). In the United Kingdom, most critical care units have clinical pharmacist input (Borthwick et al, 2023). However, throughout the rest of Europe, critical care pharmacy is still evolving, with at least 5 countries apart from the United Kingdom reporting the involvement of a critical care pharmacist (Hunfeld et al, 2024).

Several studies have been carried out using different methods to describe the role and impact of pharmacists in the ICU. Through medication reviews, pharmacists are able to identify drug-related problems (DRPs) and recommend interventions to optimise medication therapy. A drug-related problem can be defined as ‘an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes’². The role of clinical pharmacists in identifying and resolving DRPs within the ICU, together with the acceptance rate of pharmacists’ recommendations, has been studied (Johansen et al, 2016; Chapuis et al, 2019; Cvikl and Sinkovic, 2020; Chiang et al, 2021).

The role of clinical pharmacists in the ICU is varied. With knowledge of pharmacovigilance, understanding of drug dosing in the context of multiple organ failure, and pharmacological expertise, pharmacists are crucial for delivering better care in the ICU (McKenzie et al, 2024). ICU clinical pharmacists have been involved as part of the interdisciplinary critical care team, covering different fields for patient management, ranging from transitions of care (Heselmans et al, 2015; Bosma et al, 2018b), to the decrease or resolution of medication errors (Leape et al, 1999; Shulman et al, 2015), antimicrobial stewardship (Leache et al, 2020; Subedi et al, 2020), and interventions related to stress ulcer prophylaxis (Xu et al, 2021).

² Pharmaceutical Care Network Europe Association (PCNE). Classification for drug-related problems V9.1 [Online]. Basel: PCNE; 2020 [cited 2023 October 26]. Available from URL: https://www.pcne.org/upload/files/417_PCNE_classification_V9-1_final.pdf

Locally, a clinical pharmacy service was introduced in the ICU in July 2021. The service is managed by a team of clinical pharmacists who participate in daily morning ward rounds, contribute to optimising medication therapy, and collaborate on the development of ICU-specific guidelines. Rayner (2021) assessed the implementation of a pharmaceutical service in the ICU at Mater Dei Hospital (MDH). During the study, following a gap-finding exercise, the pharmacist identified pharmaceutical care issues over two months. Data relating to pharmaceutical intervention categories was presented, with an acceptance rate of 95% for the suggested interventions (Rayner, 2021).

1.4 Evaluation of clinical pharmacist contributions

One method for assessing the impact of clinical interventions by pharmacists involves gauging the clinical significance of each intervention. This can be done through the ratings given by a panel of experts using published and validated tools, including the CLEO multidimensional tool (Vo et al, 2021) and the tool by Overhage and Lukes (1999). Bosma et al (2018a) evaluated the interventions of pharmacists in the ICU, while other studies assessed the interventions of pharmacists in general hospital wards utilising one of the published tools (Bosma et al, 2008; Perez-Moreno et al, 2017; Patel et al, 2020). In the intensive care setting, information on the clinical value of direct patient care activities by pharmacists has also been reported using different tools that employ comparable scales for assessing clinical impact (Shulman et al, 2015; Richter et al, 2016).

An alternative method for evaluating a clinical pharmacy service is to assess the impact on patient outcomes. Clinical outcomes of pharmacists' interventions in the ICU include morbidity, mortality, and length of ICU stay (MacLaren et al, 2008; Marshall et al, 2008; Lee et al, 2019). Studies evaluating these outcomes include an intervention group and a control group. Conducting a study with a control group locally would not be considered ethical since the clinical pharmacy service is already functioning in the ICU.

In addition to morbidity, mortality and length of stay, the presence of a pharmacist in the ICU has been shown to optimise other clinical outcomes. Surrogate clinical endpoints have been used in literature due to difficulties associating pharmacists' interventions directly with mortality and length of stay (Kane et al, 2003). Surrogate endpoints investigated with pharmacists' interventions within the ICU include preventing ADEs (Leape et al, 1999; Kopp et al, 2007; Michalets et al, 2015; Bosma et al, 2018a), achieving therapeutic serum concentrations (Streetman et al, 2001), fluid management (Broyles et al, 1991; Branan et al, 2020; Hawkins et al, 2020; Gamble et al, 2022), medication errors (Shulman et al, 2015; Wang et al, 2015), optimisation the effectiveness and improving the safety of pharmacotherapy (Shulman et al, 2015).

One of the first studies assessing the reduction in the rate of preventable ADEs in the ICU was conducted using control and intervention groups and demonstrated that including a pharmacist in a medical ICU reduced ADEs by 66% after the intervention, while no significant change was observed for the control unit (Leape et al, 1999). Other studies evaluating pharmacists' involvement in reducing preventable ADEs include

control and intervention groups (Michalets et al, 2015), or the involvement of an expert panel to review and assess the intervention (Kopp et al, 2007; Bosma et al, 2018a). Bosma et al (2018a) studied the proportion of prevented ADEs through the interventions of critical care pharmacists. All accepted interventions in this study were given a potential ADE probability score using a previously published method (Nesbit et al, 2001), and their clinical relevance was determined by means of an expert panel. Other studies also report using the method published by Nesbit et al (2021) by means of a panel of experts in the ICU, where the clinical interventions were assessed for their likelihood of preventing an ADE in the absence of the intervention (Soakew et al 2009; Houso et al, 2022).

Fluid overload is related to poor outcomes and adverse events in critically ill patients and can impact various organs, leading to increased length of stay in the ICU, greater illness severity, acute kidney injury and increased mortality (Hawkins et al, 2020). Hidden fluids are fluids that are administered as part of routine care in the form of diluents for intravenous medications and flushes, and may account for a large volume of fluid intake in critically ill patients (Gamble et al, 2022). Fluid stewardship, aiming to prevent complications related to fluid overload, involves avoiding excess fluids, amongst other interventions, and can be led by pharmacists (Gamble et al, 2022).

In the ICU, drug dosing presents challenges due to variable pharmacokinetics, such as expanded apparent volumes of distribution owing to large volumes of fluids administered during fluid resuscitation, which may lead to suboptimal drug

concentrations, and organ dysfunction, which affects drug clearance or metabolism. Pharmacists practising in the ICU are in a unique position to advise on individual drug dosing using therapeutic drug monitoring to maximise the efficacy of medications while minimising drug toxicity (McKenzie et al, 2024). Achieving therapeutic serum concentrations for medications with a narrow therapeutic range is a goal in ICU patients and should be the standard of care for most antimicrobials (Abdul-Aziz et al, 2020). Moreover, a position paper published by an expert panel from several societies recommends routine therapeutic drug monitoring for a number of antimicrobials, including aminoglycosides, beta-lactams, vancomycin, teicoplanin and linezolid (Abdul-Aziz et al, 2020)

1.5 Quality and standardisation

Recognising the importance of pharmacist interventions in the provision of clinical pharmacy services in the ICU is a significant step. However, it is also important to consider the standards necessary to guarantee the delivery of optimal and consistent services (Wirth, 2011). Standardisation in healthcare has been shown to improve uniformity in patient care provision, enhance patient safety and minimise the risk of errors (Rozich et al, 2004; Lavelle et al, 2015). Consequently, it is important to implement standard processes to facilitate continuous quality improvement measures and ensure consistent practices among healthcare professionals to help prevent discrepancies in clinical practice.

In order to evaluate hospitals and health systems, accrediting bodies such as The Joint Commission in the United States develop standards and assess compliance with these standards and other accreditation requirements to improve the quality of care and patient safety³. In 2014, The Joint Commission of Pharmacy Practitioners developed the Pharmacists' Patient Care Process by examining key source documents relating to patient care processes⁴. The Pharmacists' Patient Care Process involves a comprehensive approach to patient-centred care that is provided together with other healthcare professionals. The ultimate goal of the Patient Care Process is to achieve standardisation of care independent of the setting where the care is being provided. Having a clearly defined and consistently implemented Patient Care Process utilised by clinical pharmacists in various practice settings is important to demonstrate reproducibility (Acquisto et al, 2021).

The Pharmacists' Patient Care Process encourages the need for a consistent process of patient care in the provision of various pharmacists' patient care services across any practice setting. The care process is provided using a five-step approach, namely, collecting necessary information, assessing and analysing the patient's medication therapy, developing a patient-centred care plan, implementing the care plan, and following up on the care plan.

³ The Joint Commission. Standards [Online]. Illinois: The Joint Commission; 2023. [cited 2023 June 28]. Available from URL: <https://www.jointcommission.org/standards/about-our-standards/>

⁴ Joint Commission of Pharmacy Practitioners (JCPP). Pharmacists' Patient Care Process [online]. United States: JCPP; 2014. [cited 2023 June 24]. Available from URL: <https://jcpp.net/patient-care-process/>

Standardisation in clinical pharmacy practice reduces unnecessary variation to improve healthcare quality and minimise the risk of errors (Acquisto et al, 2021). Institution policies and standard operating procedures incorporating process measures are an important means of standardising a specific process and involve written instructions to improve efficiency and ensure quality through uniformity of the performance of a specific task.⁵

Standards of practice for clinical pharmacists working in intensive care units in Australia, developed by the Society of Hospital Pharmacists of Australia, are available (Johnston et al, 2021). These standards outline the best practices for the delivery of pharmacy services to hospitalised patients who require intensive care. They are intended to be utilised across hospital pharmacies in Australia (Johnston et al, 2021). Similarly, in the United States, a position paper for critical care pharmacy services was developed in 2000 and updated in 2020 (Rudis and Brandl, 2000; Lat et al, 2020). Both position papers describe the scope of pharmacy services and define the activities of clinical pharmacists in the ICU. The activities of clinical pharmacists are divided into levels of service, foundational activities that are considered essential to critical care, and desirable activities that are considered 'value added' (Lat et al, 2020). While similar recommendations are not yet available in Europe, the European Society on Intensive Care Medicine (ESICM) is working on a position paper that will address the recommendations for pharmacy practice in intensive care (Hunfeld et al, 2024).

⁵ Nolen JL. Standard operating procedure [Online]. Chicago: Encyclopaedia Britannica; 2018; [cited 2023 May 28]. Available from URL: <https://www.britannica.com/topic/standard-operating-procedure>

1.6 Rationale for the study

Literature shows the value of clinical pharmacists in improving various patient outcomes. A positive perception towards clinical pharmacists' skills and valuable interventions can be observed, even though studies are mostly small single-centred studies. Institution-based evaluation and quality improvement efforts are also important (Sikora Newsome et al, 2021). Due to the recently established clinical pharmacy service in the ICU at Mater Dei Hospital, with an early indication that the pharmacist is of value in this area, a quality evaluation of the service was carried out with a focus on surrogate clinical outcomes.

1.7 Aims and objectives

The aims of this project were:

- To develop, validate and implement a quality system for service provision within the Intensive Care Unit;
- To assess the activities of clinical pharmacists in the adult Intensive Care Unit by assessing surrogate clinical outcomes.

The objectives of this research project were:

- To develop and validate a policy to standardise the activities of clinical pharmacists in the intensive care unit;

- To document and characterise pharmaceutical interventions carried out by a team of clinical pharmacists in the intensive care unit;
- To evaluate the clinical pharmaceutical interventions by assessing their impact on surrogate clinical outcomes.

Chapter 2
Methodology

2.1 Research setting

This study was carried out at the ICU at Mater Dei Hospital (MDH). The hospital is an acute general public hospital, and the ICU is a mixed unit that caters for medical, surgical, trauma and neurology critically ill patients. At Mater Dei Hospital, adult patients and paediatric patients over three years of age, requiring organ support and intensive care are admitted to the ICU, which has a capacity of 20 beds.

Ward rounds in the ICU are held twice daily and led by a consultant intensivist. A multidisciplinary team made up of clinicians, nurses, physiotherapists, and clinical pharmacists participate during the morning ward rounds. A team of clinical pharmacists actively participates in ICU interdisciplinary morning ward rounds and is available on the unit seven days per week during the morning hours. The team is made up of four pharmacists who attend ICU ward rounds on a rotating basis. One or two pharmacists are available at the ICU, and the other pharmacists are either off-duty or engaged in other responsibilities. This system ensures ICU ward rounds are covered seven days a week.

The responsibilities of the pharmacists encompass medication chart review for patients admitted to the ICU on a daily basis, provision of medicine information and instructions for the administration of parenteral and enteral medications. Other tasks include updating the patient profiles before and after each ward round, documentation of pharmaceutical interventions (PIs), and liaising with pharmaceutical departments

regarding matters directly related to patient care. Pharmacists incorporate all the interventions carried out during each ward round in the patient profiles, which are electronically saved in a shared online folder.

2.2 Research design

The research was conducted in two phases. The first phase involved the development and validation of a hospital policy to standardise the activities of clinical pharmacists in the ICU. The second phase involved the development of a data collection tool to capture, classify and evaluate the pharmaceutical interventions of clinical pharmacists in the ICU. This was followed by the collection of data relating to pharmaceutical interventions over a period of three months and their evaluation by an expert panel of healthcare professionals. Prior to the initiation of the research study, approval was granted by the data protection office of Mater Dei Hospital, and ethical approval was granted by the University Research Ethics Committee (Appendix 1).

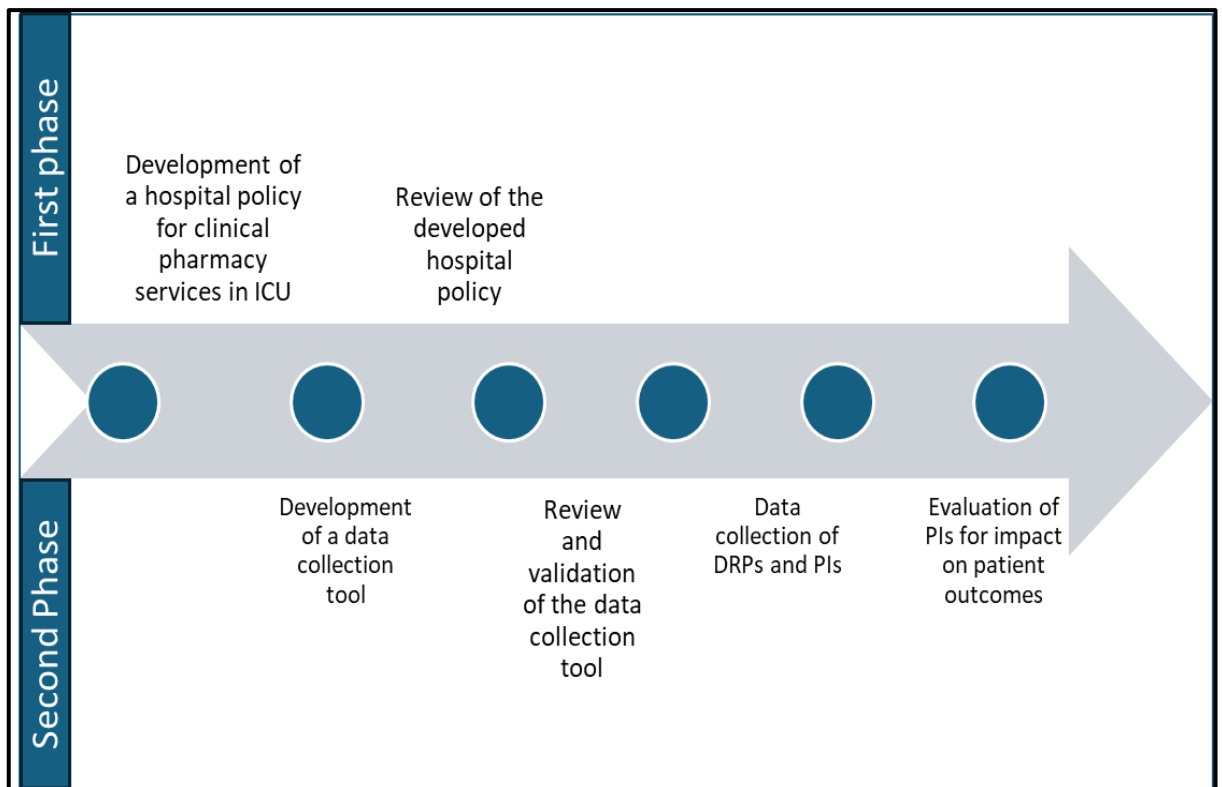


Figure 2.1: Research design timeline

DRPs Drug-Related Problems; PIs Pharmaceutical Interventions; ICU Intensive Care Unit

2.3 Policy development

The purpose of the policy is to identify and describe the scope of practice of clinical pharmacy services in the intensive care, thus standardising pharmaceutical activities in the ICU. Literature was reviewed for best practices for clinical pharmacists practising in the ICU. The position paper on Critical Care Pharmacy Services developed by the American College of Clinical Pharmacy (ACCP) and the Society of Critical Care Medicine (SCCM), the Guidelines for the provision of Intensive Care Services by the Faculty of

Intensive Care Medicine and Intensive Care Society⁶, and the Standard of practice in intensive care for pharmacy service by the Society of Hospital Pharmacists of Australia (SHPA) were considered to gain insights into the fundamental activities of critical care pharmacists and extract key points to develop a local policy (Rudis and Brandl, 2000; Johnston et al, 2021). These guidelines and standards were selected since they comprehensively discuss the critical care pharmacists' role and activities. The Pharmacist Patient Care process was chosen to provide insight into a patient-centred approach during the pharmacists' activities when providing patient care⁷. Daily tasks carried out by pharmacists practising in other ICUs across Europe were also considered to compare the clinical pharmacy service being delivered locally to practices in other European countries where the clinical pharmacy service is developing (Hunfeld et al, 2024).

2.3.1 Policy content

The policy, entitled 'Policy on Clinical Pharmacy Services Provision within the Intensive Care Unit,' was developed (Appendix 2). It is divided into activities that focus on direct patient care and those activities relating to indirect patient care. Direct patient care encompasses the delivery of pharmaceutical care to optimise medication use and improve patient outcomes. This is achieved through pharmacists' participation in interdisciplinary ward rounds, medication chart reviews, provision of medicines

⁶ The Faculty of Intensive Care Medicine (FICM), The Intensive Care Society (ICS). Guidelines for the Provision of Intensive Care Services [Internet]. London: FICM and ICS, 2022. [cited 2023 May 28]. Available from URL: <https://ics.ac.uk/resource/gpics-v2-1.html>

⁷ Joint Commission of Pharmacy Practitioners (JCPP). Pharmacists' Patient Care Process [online]. United States: JCPP; 2014. [cited 2023 June 24]. Available from URL: <https://jcpp.net/patient-care-process/>

information, monitoring medication therapy, optimisation of medication dosing, optimisation of medication administration, and documentation of clinical activities. Indirect patient care involves activities relating to quality improvement in intensive care, comprising of reporting adverse drug reactions, reporting patient safety issues, and contributing to the development and updating of guidelines and drug monographs relevant to medication use in the ICU.

The policy encompasses the roles and responsibilities of the team of pharmacists providing a clinical pharmacy service in the ICU together with the responsibilities of the interdisciplinary team. The functions of the pharmacy team providing clinical pharmacy services in the ICU are described in detail in the developed policy and are divided into fundamental activities and recommended activities based on the criticality of patient care.

2.3.2 Policy structure

The Policy was written on the Mater Dei Hospital template for policies, using the same format and structure as for other policies issued by the hospital, as described in Figure 2.2. The first page contains information about the policy owner, the policy author, the groups consulted for policy development, policy reviewers, and the management team giving the final approval. Dates related to approval and next review, together with version numbers, are also included on the first page.

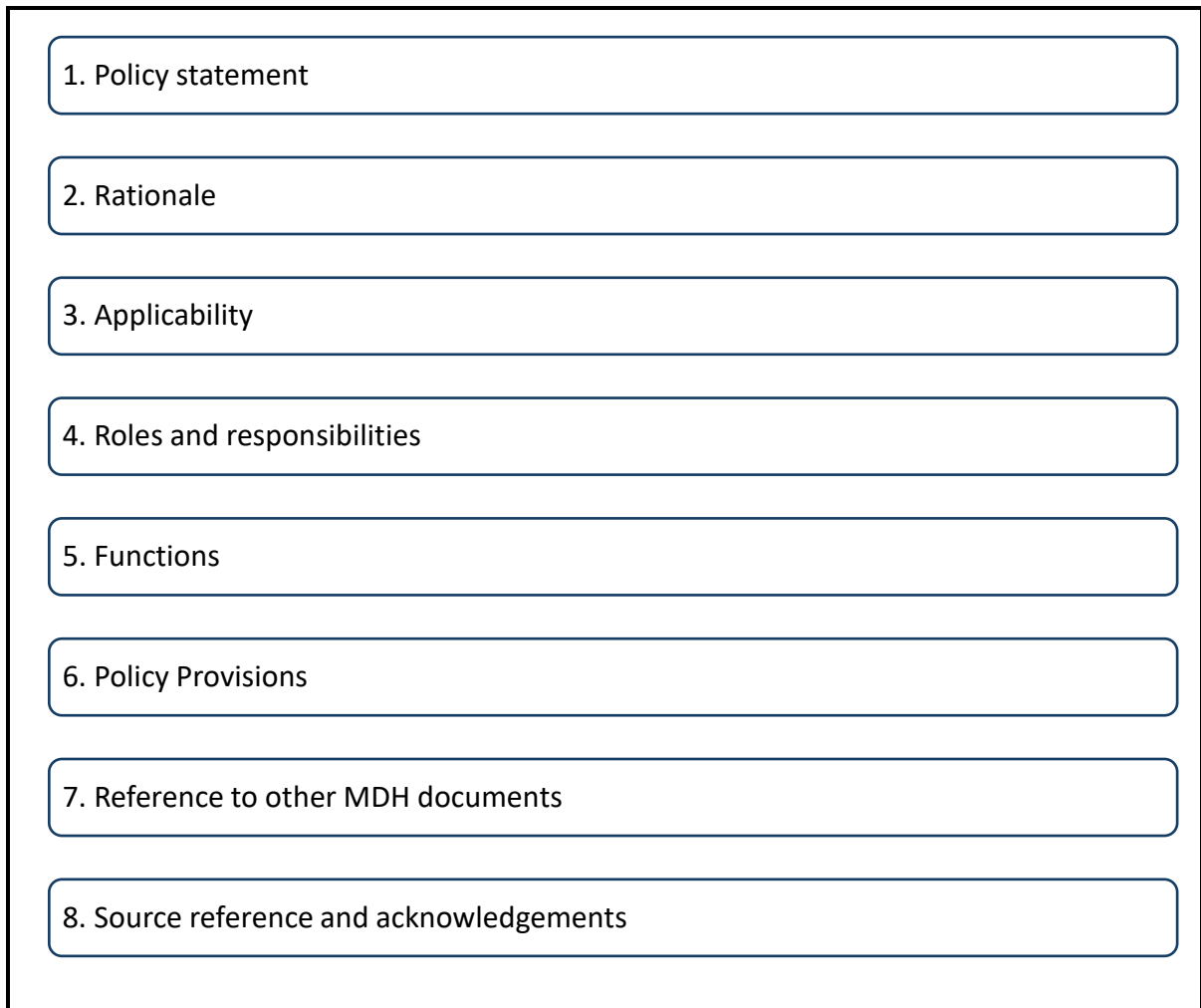


Figure 2.2: Sections of the developed policy

MDH Mater Dei Hospital

2.3.3 Policy review and validation

The developed policy was reviewed and validated for its relevance, appropriateness and practicality in the ICU and evaluated through a multi-level approach by an expert panel of healthcare professionals. The panel's review assisted in confirming that the responsibilities and functions of pharmacists set out in the policy were comprehensive and aligned with ensuring patient safety. The panel of experts consisted of healthcare professionals from the hospital pharmacy and the ICU. The pharmacist heading the

quality improvement section at Mater Dei Hospital Pharmacy was the healthcare professional consulted about policy development. Three clinical pharmacists practising in the ICU carried out internal validation of the policy. Three ICU nursing officers and a consultant intensivist, who are external to the pharmacy directorate, but have clinical experience in the ICU, also reviewed the developed policy.

All healthcare professionals reviewing the policy were handed a copy of the information letter explaining details about the study and a consent form for healthcare professionals. The initial step involved a number of constructive discussions between the pharmacist researcher developing the policy and the pharmacist heading the quality improvement section within the Pharmacy Directorate at MDH. Agreements were reached, and the necessary adjustments were implemented to shape the policy. The members of the expert panel were approached by the pharmacist researcher and given an explanation of the policy requirements. They were asked to review the policy in terms of clarity, comprehensiveness, and feasibility and encouraged to include any additional comments and suggestions. The clinical pharmacists practising in the ICU were invited to voice their agreement or otherwise regarding task prioritisation and to subsequently discuss recommendations with the pharmacist researcher. Discussions were held with the internal validators, leading to consensus and fine-tuning of the policy based on proposed feedback. Reviewers external to the pharmacy directorate provided written feedback, which was taken into account. The needs of the local ICU and the constraints posed by limited resources were carefully considered when developing and reviewing the policy.

The activities of pharmacists practising in the ICU were expanded as a result of discussion with members of the expert panel. Priorities of activities of the clinical pharmacy team were discussed and agreed upon with the expert panel.

2.4 Development of the data collection tool

A data collection tool was developed and validated to capture DRPs, categorise subsequent PIs and facilitate the evaluation of PIs in terms of their impact on patient outcomes (Appendix 3). The development of such a tool was important for achieving standardised and systematic classification of DRPs and PIs, as well as enabling a standardised assessment of PIs' influence on patient outcomes. The tool needed to be robust enough to capture all DRPs while also enabling a systematic evaluation of PIs by an expert panel of healthcare professionals.

A classification system based on the PCNE V9.1⁸ was identified to capture DRPs in the ICU. This classification system offers extensive categories for identifying and categorising DRPs and has been used in other studies (Eichenberger et al, 2010; Martins et al, 2019; Ayhan et al, 2022; Dong et al, 2022). A published and validated score for evaluating PIs in preventing a potential ADE was selected to assess the likelihood of an ADE occurring in the absence of the suggested and implemented PI (Nesbit et al, 2001). This score was

⁸ Pharmaceutical Care Network Europe Association (PCNE). Classification for drug-related problems V9.1 [Online]. Basel: PCNE; 2020 [cited 2023 October 26]. Available from URL: https://www.pcne.org/upload/files/417_PCNE_classification_V9-1_final.pdf

chosen because it has been employed in published studies and provides a practical framework for evaluating PIs (Saokaew et al, 2009; Gallagher et al, 2014; Kearney et al, 2017; Bosma et al, 2018a; Bosma et al, 2018b; Dong et al, 2022; Wilkes et al, 2022).

An initial section was included in the data collection tool, containing patient demographics, comprehensive textual information about context, the background of the patient and details of the drug-related problem and the suggested pharmaceutical intervention. Patient demographics included gender, age bracket, weight, height, creatinine clearance, dialysis mode, and other pertinent laboratory results since these were perceived relevant by the pharmacist researcher to comprehend the context of the patient's clinical status and the associated DRP and PI.

The categorisation of DRP and PI was included along with the classification of medication corresponding to the first level of the Anatomical Therapeutic Chemical (ATC) classification system. The cause of DRPs was based on the categorisation system published by the PCNE V9.1, which was modified to reflect the local ICU setting. Modifications to the DRP classification included changes to causes pertaining to DRP categories and the addition of a new DRP category, 'Monitoring', as described in Table 2.1.

Table 2.1: Modifications to the DRP classification to adapt it to the ICU setting

Modified DRP category	Modifications carried out
Dispensing Category	Two causes, 'necessary information not provided or incorrect advice provided' and 'wrong drug, strength or dosage advised', were removed since they were mainly related to OTC medication and, thus, considered not relevant to the in-patient setting.
Patient-related Category	The cause 'patient physically unable to use drug/form as directed' was retained, whilst the other nine causes were removed as they were deemed irrelevant to the ICU setting.
Patient transfer-related Category	The cause 'medicine reconciliation problem' was divided into two causes to differentiate DRPs upon admission to the ICU and DRPs upon patient transfer out of the ICU; one cause pertains to the 'medicine reconciliation problem upon admission to the ICU', whereas the other cause relates to the same problem upon patient transfer out of the ICU.
Others Category	In the PCNE classification for DRPs, 'No or inappropriate outcome monitoring including TDM' is part of the category 'Others'. Monitoring is perceived as important in an ICU setting. Thus, a new Category, 'Monitoring', was added, comprising 2 causes, 'Therapeutic drug monitoring required' and 'Other monitoring need', as these causes were considered to be significant, whereas the category 'Others' was removed.

OTC Over the counter; ICU intensive care unit; DRPs Drug-related problems; PCNE Pharmaceutical Care Network Europe; TDM therapeutic drug monitoring

In the subsequent section of the data collection tool, PIs to be suggested by clinical pharmacists, which are directly related to the DPRs identified, were included. The PIs encompassed seven main categories associated with DRPs, namely, 'Change medication',

'Dose adjustment', 'Change in formulation or administration route', 'Change in instructions for drug administration', 'Discontinue or pause medication', 'Addition of a medication', and 'Monitoring need'. Furthermore, the medications implicated in DRPs and PIs are categorised according to the ATC classification, first level, in the following section of the data collection tool as detailed in Figure 2.3.

The final part of the data collection tool involves the evaluation of PIs in their ability to prevent a potential ADE (pADE) together with documentation about the impact on different patient outcomes. The score used for the evaluation of PIs contains five probability score categories; high (0.6), medium (0.4), low (0.1), very low (0.01) and zero (0) probability of preventing a potential ADE. Each category contains an explanation of the probability and examples of interventions or drug-related problems falling into each respective category, which were generated from published literature (Saokaew et al, 2009; Gallagher et al, 2014; Kearney et al, 2017; Bosma et al, 2018b; Dong et al, 2022; Houso et al, 2022; Wilkes et al, 2022). The impact of the PI is related to 4 outcomes, namely, the potential prevention of a pADE, assisting in fluid management, achieving therapeutic concentrations for medications with a narrow therapeutic range, or therapeutic optimisation. Therapeutic optimisation is defined as a proactive contribution that seeks to enhance patient care (Shulman et al, 2015).

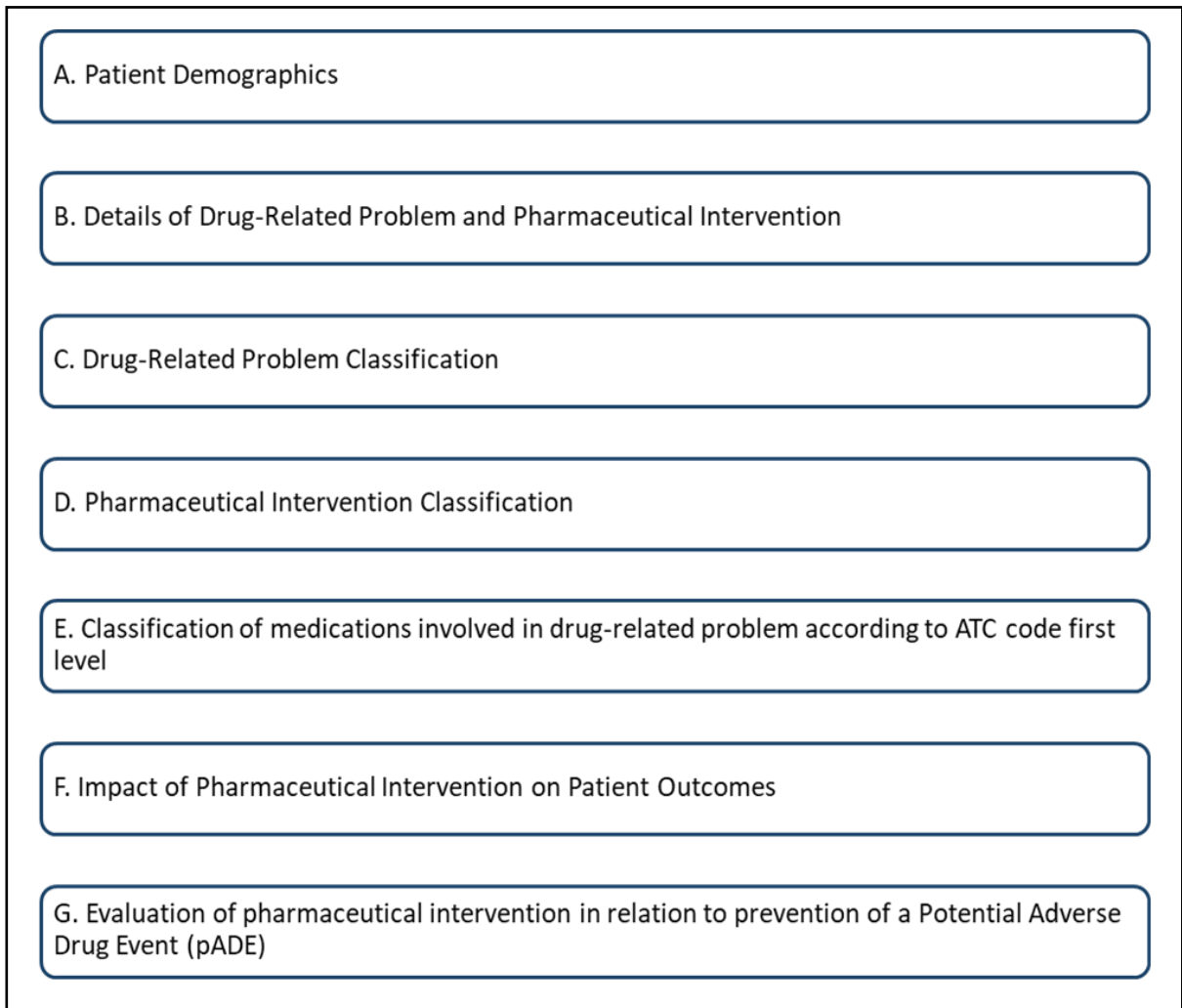


Figure 2.3 Sections of the Data Collection Tool

ATC Anatomical Therapeutic Chemical; pADE Potential Adverse Drug Event

2.4.1 Data collection tool review and validation

The data collection tool underwent evaluation for face and content validity by an expert panel of healthcare professionals made up of three pharmacists practising in the ICU and one consultant intensivist. The panel of experts were asked to validate the tool for clarity, relevance and appropriateness of each section and category. The members of the panel

were approached by the pharmacist researcher and given an explanation relating to the tool requirements and its application. They were presented with questions to state their views about the data collection tool (Appendix 4). This process aimed to address the following aspects:

Assessing whether the patient demographics section had sufficient details,

Assessing whether the textual description relating to details of background, DRP and PI is comprehensive;

Assessing whether the classifications of DRPs were satisfactory, specifically whether any categories or descriptions necessitated to be included, modified or omitted;

Assessing if the categories and descriptions of PIs proposed by pharmacist researcher were appropriate and comprehensive, and whether any categories or descriptions needed to be included, amended or omitted;

Whether the classification according to the ATC classification system being used was appropriate;

Whether the pADE score with description was clear and comprehensive, and if more examples from literature were to be included;

Whether the section about the impact of PI on patient outcomes was clear enough.

Following validation and incorporating the feedback proposed by the expert panel, the tool was piloted in the ICU for the initial 10 days, corresponding to approximately 10% of the study period (Connelly, 2008). During the pilot study, the data collection tool was utilised to document and categorise all identified DRPs and suggested PIs, which were

subsequently assessed by the expert panel in order to test the feasibility and practicality of the tool. The pilot study included interventions on patients who met the inclusion criteria for the research study. Subsequently, the tool was further adapted to the ICU setting based on insights gained during the pilot phase, with minor adjustments made to the layout and the classification section.

2.5 Data collection

2.5.1 Sampling strategy and inclusion criteria

Convenience sampling of patients admitted to the ICU during the study period of three months between September and December 2023 was performed. Adult patients over 18 years of age admitted to the ICU during the research period whose treatment chart was reviewed by pharmacists were considered.

2.5.2 Method of data collection

Data was collected following the necessary Ethical approval from the University of Malta Research Ethics Committee (Appendix 1). During this phase, all the pharmaceutical interventions carried out by a team of pharmacists practising in the ICU that were related to a drug-related problem were considered in line with the inclusion criteria. For the

purpose of this study, data was extracted daily from the saved patient profiles, with the assistance of an intermediary who pseudonymised the patient data.

The four pharmacists participating in data collection have been practising in the ICU for between one and three years and follow ICU-specific guidelines and protocols for their daily work. Most drug-related problems are identified during the morning interdisciplinary ward rounds and medication chart reviews. For each DRP identified, the pharmacists recommend a pharmaceutical intervention, which is communicated verbally to the ICU clinicians or ICU nurses, depending on the intervention. DRPs and PIs are documented in the patient profile available during the ward round and later updated and saved in the departmental folder. Anonymised patient profiles were made available for this research study, where the pharmacist researcher extracted patient demographics and clinical background, background of DRP and PI, and completed a data collection sheet for each intervention. Each intervention that arose due to a DRP was considered. A comprehensive textual description was documented for each DRP and PI, together with the patient's demographics and relevant clinical details. DRPs and PIs were categorised based on the classification outlined in the data collection sheet. Additionally, the medications associated with the DRP were classified according to their ATC code first level. One PI was possible for each DRP.

The section in the data collection tool relating to the impact of the intervention on patient outcomes was completed with the best possible outcome, specifically if the intervention was associated with the prevention of a potential ADE, fluid management,

achieving therapeutic concentrations for medications with a narrow therapeutic range, or therapeutic optimisation. A number of interventions could affect more than one patient outcome.

2.5.3 Evaluation of pharmaceutical interventions in relation to the prevention of a potential adverse drug event (pADE)

The final section of the data collection tool focused on the evaluation of each pharmaceutical intervention in relation to preventing a potential ADE, and the severity of the potential ADE in the absence of the intervention. This evaluation was carried out by an expert panel made up of a consultant intensivist who has been practising in the ICU for 10 years and a clinical pharmacist with more than two years of ICU experience. Both healthcare professionals were provided with a concise overview of the study and a detailed explanation of potential ADEs, and subsequently, they familiarised themselves with the data collection tool.

During the evaluation process, all interventions carried out by pharmacists were presented to the expert panel of healthcare professionals in an anonymised manner, utilising the data collection tool. The panel of experts was external to the research study. The two assessors, working independently, evaluated each intervention and assigned a pADE score, based on the clinical data of the patient. The expert panel utilised the data collection tool developed using the Nesbit method and their professional judgment for evaluating clinical interventions (Nesbit et al, 2001). Each intervention was given a score

in relation to the probability of an ADE occurring in the absence of the pharmaceutical intervention. The intervention could have a score of zero, which indicated no harm was expected, very low, indicating some harm was expected but not clinically relevant, low, indicating some harm was expected but poorly clinically relevant, medium, indicating that harm was expected and it was clinically relevant, or high indicating that severe or life-threatening harm was expected. In those cases where interventions were assigned different scores during the expert panel evaluation, consensus was reached through a separate discussion among the panel members.

2.5.4 Data analysis

Anonymised data related to patients, prescriptions, DRPs and PIs were recorded into a Microsoft Excel spreadsheet (Version 2404). Characteristics of DRPs and PIs were described by percentage and frequency. Descriptive statistics included the median for patient age, number of DRPs per patient, and standard deviation for the number of DRPs per patient.

2.6 Dissemination of findings

A poster presentation entitled 'Development and Validation of a Data Collection Tool to Evaluate Pharmaceutical Interventions in the Intensive Care Unit' was presented at the

28th Congress of the European Society of Hospital Pharmacists in Bordeaux, France, in March 2024 (Appendix 5).

An abstract entitled 'Evaluation of Pharmaceutical Interventions in an Intensive Care Unit' was accepted as a poster presentation at the 82nd FIP World Congress of Pharmacy and Pharmaceutical Sciences in Cape Town, South Africa, to be presented in September 2024 (Appendix 5).

Chapter 3

Results

3.1 Policy development and validation

Through constructive discussions and feedback, the activities of pharmacists in the ICU presented in the developed policy were expanded. An additional activity, involving documentation of specific pharmacotherapeutic recommendations in the patient's medical notes, was incorporated into the policy upon discussion with the pharmacist responsible for quality improvement. Reviewers believed that this activity would facilitate communication with the entire patient care team.

The members of the expert panel provided positive feedback about the policy. The policy was deemed to be appropriate for its intended purpose, comprehensive, and provides guidance and consistency to the clinical pharmacy service. The roles and responsibilities of the team were enhanced following discussions with the panel as described in Table 3.1. Due to the various activities that the pharmacists need to carry out when present on the ward, the policy developer, the pharmacist heading the quality improvement section, the expert panel, and the director of pharmacy reached a consensus about prioritisation of pharmacist activities in the ICU, considering the limited resources of the pharmacy team and the needs of clinical pharmacy service.

Table 3.1: Improvements in policy after expert panel review

Criteria for improvement	Expert panel suggestions
Modification of activities carried out by pharmacists	Splitting the function relating to reporting adverse drug events and patient safety events into two separate functions; one for reporting adverse drug events and one for reporting patient safety events, since they are reported to separate authorities, and elaborating more on each function to provide clarity
	Inclusion of a systematic process in the function related to the development of guidelines and monographs, thus ensuring a more structured approach and consistency
	Revising the function related to participation in morning ward rounds and patient chart reviews, making it more concise to streamline the process
Additional activities	Introduction of a new activity to document pharmacotherapeutic recommendations by pharmacists in the patients' medical notes to enhance communication with the entire healthcare team
Prioritisation of activities	Discussions with the pharmacist responsible for quality improvement, feedback from internal validators, consensus by reviewers external to the pharmacy directorate, and final approval by management to prioritise crucial activities of pharmacists practising in the ICU
	Both direct and indirect patient care activities were divided into essential and recommended activities, depending on their criticality for the safe provision of pharmaceutical care to patients in the ICU

The final policy (Appendix 2) includes eleven functions of the clinical pharmacy team, divided into those associated with direct patient care and indirect patient care. The eleven functions are further categorised as essential activities and recommended activities as described in Table 3.2. Classification of functions into essential and recommended activities resulted from discussions with the pharmacist responsible for quality improvement, insightful feedback from the internal validators, agreement by reviewers external to the pharmacy directorate, and approval by the director of pharmacy.

Essential activities refer to direct patient care activities that are crucial for ensuring the safe provision of pharmaceutical care to patients who are critically ill and indirect patient care activities that are fundamental for the safe continuity of clinical pharmacy service. Recommended activities describe direct patient care activities that are desirable within the ICU environment and are carried out in addition to the essential activities directly related to patient care. Recommended activities also comprise those indirect patient care activities that are necessary for maintaining the continuity of the clinical pharmacy services and are carried out in addition to all other essential and recommended activities.

The developed policy has now been incorporated within the MDH pharmacy directorate following approval from management.

Table 3.2: Essential and recommended activities of pharmacists within the ICU

Direct patient Care		Indirect Patient Care	
Essential Activities	Recommended Activities	Essential Activities	Recommended Activities
Participation in daily morning ward rounds and/or medication chart review	Updating patient profiles prior to ward round	Reporting Patient Safety Events	Documentation of clinical activities and pharmaceutical interventions
Provision of medicine information and administration instructions to healthcare professionals in the ICU	Medication chart review for patients transitioning out of ICU	Reporting Adverse Drug Reactions (ADRs)	Development and update of guidelines and monographs
Liaison with pharmaceutical departments concerning matters directly related to patient care	Documentation of specific pharmacotherapeutic recommendations in the patient's medical notes		
Update of patient profiles following ward round			

3.2 Data collection tool development and validation

The data collection tool was positively evaluated and deemed to be clear, relevant and appropriate for its intended use in the ICU. Suggestions put forward by the expert panel were:

Include relevant drug history, pertinent past medical history and relevant allergies within the initial sections since the intervention could be related to these clinical issues. This concept is addressed in the section of the data collection tool 'Details of Drug-related problem and Pharmaceutical intervention', within the background subsection.

Add a new cause for the category 'Drug Form' in the DRP classification section to include more suitable routes of administration. The added cause is entitled 'Another drug formulation/ route of administration more appropriate for this patient'.

Rephrase the cause 'Wrong drug or strength dispensed' within the Dispensing Category of the DRP Classification section to 'Wrong drug or strength made available at ward'.

Add a new cause for the category 'Drug use process' in the DRP classification section to include wrong or inappropriate methods of administration when the route of administration is right, but the method is inappropriate. This cause applies to both the parenteral and enteral route. The added cause is entitled 'Inappropriate parenteral/enteral drug administration method'.

Add a new DRP category called 'Identification of Adverse Effects' with two causes; 'Identification of adverse drug event' and 'Identification of adverse drug reaction'.

Rephrase the PI category within the PI classification section, 'Addition of a new medication', to 'addition of a medication' since this category could be used for interventions related to restarting medications that had been paused, which are not new medications.

Include more examples from literature for each category in the section relating to the evaluation of PI in relation to the prevention of a potential ADE, as this would help the expert panel gain a clearer understanding of the impact of specific interventions.

Assign numerical labels to the different sections of the data collection tool to enhance clarity and organisation.

During the pilot study over 10 days, where the data collection tool was employed to document DRPs and PIs, a need arose for another cause for the category 'Drug Selection' within the DRP classification section related to the medications that are contraindicated or to be used with caution in specific patients. This additional cause was entitled 'Inappropriate medication based on the patient's clinical status'. The layout of the data collection tool was improved to enhance usability for the expert panel and facilitate the evaluation of the intervention in relation to preventing a potential ADE.

3.3 Data collection

Over three months, 197 patients were admitted to the ICU. Data from 164 patients was considered for this research study, in line with the inclusion criteria, including patients over 18 years of age whose medication chart was reviewed by the pharmacists. Of these patients, 94 (57%) were males and 70 (43%) were females, as shown in Table 3.3. The age group with the highest frequency was between 70 and 79 years, whereas the mean age fell within the 60 to 69 years bracket. The length of stay at ICU ranged between 1 and 33 days, with a mean length of stay of 7 days. Four patients were re-admitted during the study period, and these instances were considered as the same patient, although under a different admission.

A total of 484 drug-related problems were identified by pharmacists during the study period. This resulted in a mean of 2.9 DRPs per patient, with the frequency of DPRs per patient ranging from zero to 18. Out of 164 patients included in the study, 135 patients had at least one DRP as highlighted in Table 3.3.

Table 3.3: Patient demographics and prevalence of DRPs (N=164)

	Total
Patients admitted to the ICU	197
Patients included in the study	164 (100%)
Males	94 (57%)
Females	70 (43%)
Mean Age	60-69 years
Patients with at least one DRP	135 (82%)
Patients without DRPs	29 (18%)
Mean number of DRPs per patient included in the study N=164	2.9 ± 3.2*

* Mean ± standard deviation

3.3.1 Classification of drug-related problems (DRPs)

The identified DRPs were categorised corresponding to the classification system in the data collection tool, as described in Figure 3.1. The most commonly identified DRPs were related to dose selection (n=186 (38%)), drug selection (n=115 (24%)), monitoring (n=65 (13%)), and drug use process/drug administration (n=58 (12%)).

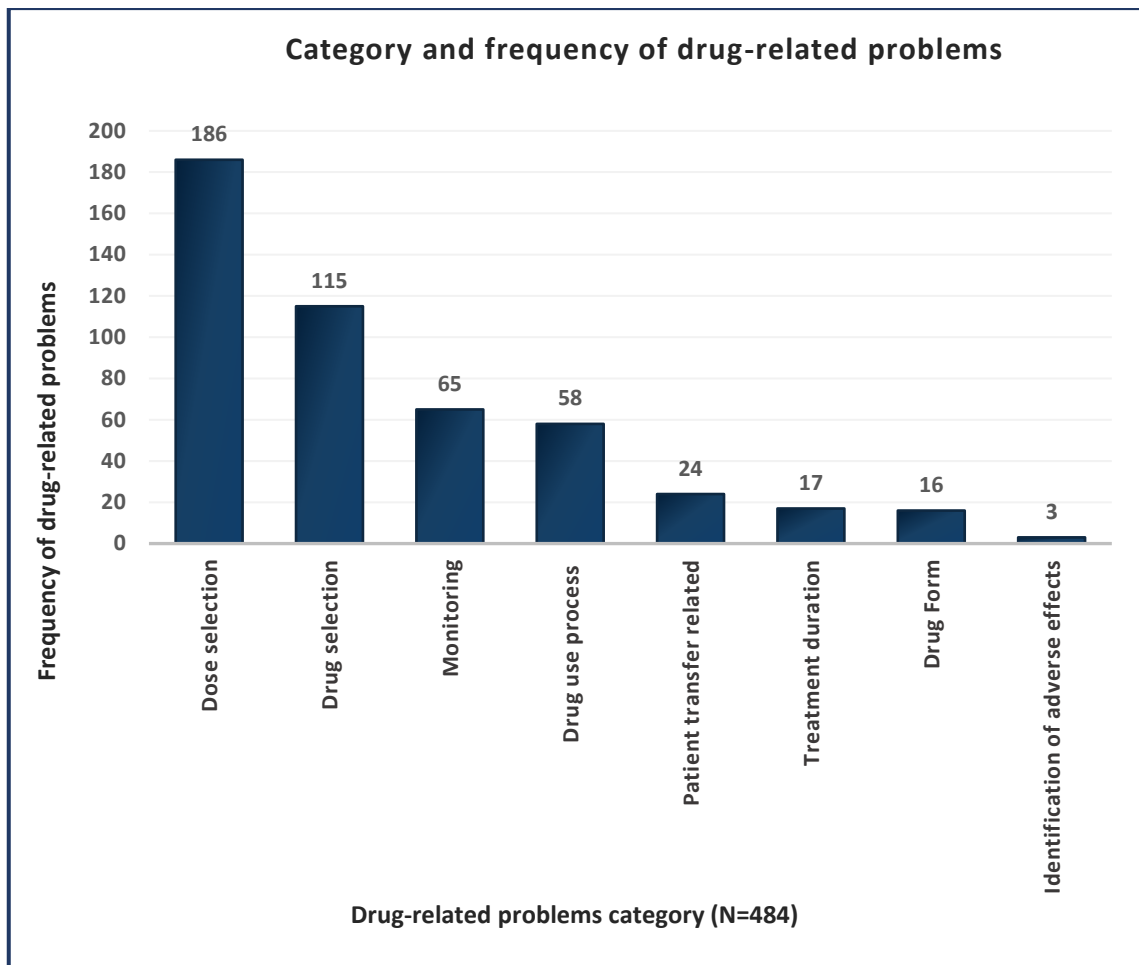


Figure 3.1: Category and frequency of drug-related problems identified in 164 patients (N=484)

The ‘**Dose selection**’ category comprised five possible causes, as outlined in Table 3.4. Within this category, DRPs occurred due to daily doses that were either too high or too low for the patient’s clinical condition, including changes in renal function, hepatic function, and weight. Additionally, DRPs arose due to dosage regimens that were either too frequent or not frequent enough for the patient’s clinical status, as well as dose timing instructions that were wrong, unclear, or missing.

Table 3.4: Dose selection category

Causes (n=186)	Frequency of DRPs
Dosage regimen not frequent enough	43
Dosage regimen too frequent	43
Drug dose of a single active ingredient too high	42
Drug dose too low	34
Dose timing instructions wrong, unclear or missing	24

DRPs identified within the '**Drug selection**' category were related to six causes, as detailed in Table 3.5. No DRPs were identified for the cause 'Too many drugs/active ingredients prescribed for indication'. For the 'Drug Selection' category, DRPs occurred mostly due to 'incomplete drug treatment despite existing indication', which ranges from incomplete stress ulcer prophylaxis, incomplete electrolyte replacement, and incomplete supplementation for patients with refeeding syndrome to incomplete PCP prophylaxis in an immunocompromised patient. Moreover, DRPs also arose from 'inappropriate medication based on the patient's clinical status', 'inappropriate combination of medications,' 'inappropriate duplication of the therapeutic group or active ingredient', 'inappropriate drug according to guidelines/formulary', and 'no indication for drug'.

Table 3.5: Drug selection category

Causes (n=115)	Frequency of DRPs
No or incomplete drug treatment despite existing indication	61
Inappropriate medication based on the patient's clinical status	23
Inappropriate combination of medications	21
Inappropriate duplication of therapeutic group or active ingredient	5
Inappropriate medication according to guidelines/formulary	4
No indication for drug	1
Too many different drugs/ active ingredients prescribed for indication	0

The '**Monitoring**' category incorporated the need for therapeutic drug monitoring for medications with a narrow therapeutic range or a high degree of nephrotoxicity, together with the need for other monitoring. Out of 65 DRPs within this category, 62 were related to therapeutic drug monitoring, and 3 were related to other monitoring need.

The '**Drug use process**' category relates to drug administration by healthcare professionals and encompasses seven causes, as described in Table 3.6. This category mostly involves DRPs due to the cause 'Inappropriate parenteral/ enteral drug administration method' such as those related to using an inappropriate diluent for parenteral medications, inappropriate volume of diluent, or inappropriate infusion rate.

Other causes within this category comprise ‘inappropriate timing of administration or dosing intervals by a healthcare professional’, a drug that has been ‘over-administered’ or ‘under-administered by a healthcare professional’, or ‘drug not administered at all by a healthcare professional’. No DRPs were identified for the causes relating to administration of a wrong drug or administration via the wrong route by a healthcare professional.

Table 3.6: Drug use process category

Causes (n=58)	Frequency of DRPs
Inappropriate parenteral drug administration method	39
Drug under-administered by a healthcare professional	7
Inappropriate timing of administration or dosing intervals by a healthcare professional	6
Drug not administered at all by a healthcare professional	5
Drug over-administered by a healthcare professional	1
Wrong drug administered by a healthcare professional	0
Drug administered via the wrong route by a healthcare professional	0

The ‘**Patient transfer-related category**’ pertains to DRPs identified during patient admission to the ICU or during patient transfer out of the ICU to general hospital wards. These DRPs may include the need to continue home medications or may involve

stopping or gradually tapering medications initiated in the ICU and restarting medications as necessary. The frequency of DRPs in this category is detailed in Table 3.7.

Table 3.7: Patient transfer-related category

Causes (n=24)	Frequency of DRPs
Medication reconciliation problem upon admission to ICU – medications that need to be continued/stopped upon admission	13
Medication reconciliation problem upon patient transfer from ICU – medications that need to be continued/stopped/changed upon transfer	11

The '**Treatment duration category**' encompasses DRPs in which the duration of treatment is too long or too short. Out of 17 DRPs identified in this category, 2 were related to a short duration of treatment, while 15 resulted from a long duration of treatment.

DRPs identified within the '**Drug form**' category (n=16) were related to issues with the formulation of the drug and were associated with two specific causes, 10 resulted from 'inappropriate drug form/formulation for this patient', whereas 3 DRPs were related to the cause 'another drug formulation /route of administration more appropriate for this patient'.

There were three DRPs within the category '**Identification of adverse effects**'. Specifically, one DRP involved the identification of thrombocytopenia as an adverse effect of treatment with sodium valproate. This occurred for a patient who had been initiated on sodium valproate during ICU admission. The other interventions involved the identification of a prolonged QT interval as an ADE of levofloxacin and the attribution of dilated pupils to atropine.

3.3.2 Pharmaceutical interventions

For each identified DRP during ICU ward rounds and medication chart review by pharmacists, the pharmacist present at the ICU suggested a pharmaceutical intervention. The PIs were classified based on the developed data collection tool and are presented in Figure 3.2. The pharmacists practising in the ICU intervened mostly in medication dose adjustments (40% (n=193)), the addition of medications (17% (n=80)), and monitoring (16% (n=79)).

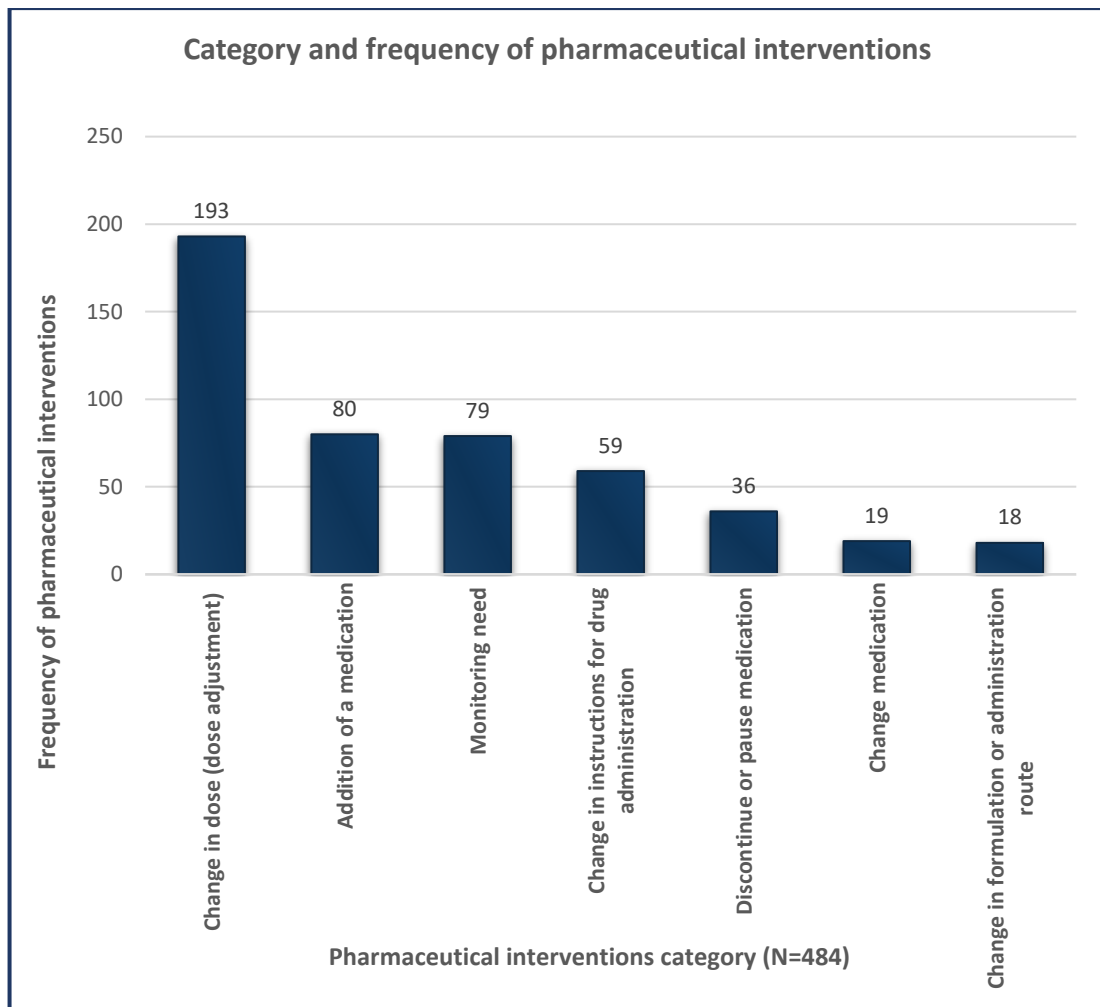


Figure 3.2: Category and frequency of pharmaceutical interventions suggested by pharmacists

3.3.2.1 Dose adjustment

This category encompasses all interventions related to changes in medication doses. The majority of interventions were related to the 'Dose Selection' DRP category, where 185 DRPs out of a total of 186 in this Category led to a dose adjustment. Additionally, DRPs from other categories also resulted in dose adjustment interventions. Further details of such DRPs and PIs are provided in Table 3.8.

Table 3.8: Dose adjustment category – examples and frequency

DRP category	Number of DRPs	Example of DRP	Examples of the PI category 'Dose Adjustment' (n= 193)
Dose selection	185	The dose of piperacillin and tazobactam is currently at 4.5g 12-hourly due to previous AKI. The patient's renal function has improved, and current Creatinine Clearance is 32 mL/min	The pharmacist advised increasing the daily dose of piperacillin + tazobactam to 4.5g 8-hourly due to improving renal function
Duration of treatment	2	Omeprazole infusion 8 mg/hour has been prescribed for more than 72 hours due to major peptic ulcer bleeding	The pharmacist advised to stop the infusion after 72 hours and reduce the dose to 40 mg twice daily
Identification of adverse effects	1	Identification of thrombocytopenia related to treatment with sodium valproate	The pharmacist advised to decrease the dose of sodium valproate gradually to minimise the risk of seizures (and add another antiepileptic – levetiracetam)
Drug selection	3	Drug-drug interaction between clarithromycin 500 mg 12-hourly and atorvastatin 40 mg once daily	The pharmacist advised lowering the dose of atorvastatin to a maximum of 20 mg once daily while the patient is being treated with clarithromycin.
Patient-transfer related	2	A patient had been started on intermittent morphine oral solution following continuous infusion. The patient is being transferred out of the ICU, and there is no plan to taper down the morphine	The pharmacist advised a plan to taper down the dose of morphine gradually in the general ward until morphine is stopped.

AKI Acute kidney injury

3.3.2.2 Addition of a medication

The 'Addition of a medication' category relates to pharmaceutical interventions that propose either adding new treatment or restarting previous medications. DRPs from categories relating to drug selection, treatment duration, and those which are related to patient transfer resulted in interventions involving addition or restarting medications, for which examples are shown in Table 3.9.

Table 3.9: Addition of a medication category – examples and frequency

DRP category	Number of DRPs	Example of DRP	Examples of the PI category 'Addition of a medication' (n=80)
Drug selection	61	A patient has been started on high-dose corticosteroids and was also intubated. No stress ulcer prophylaxis was prescribed.	According to local ICU guidelines, the patient requires stress ulcer prophylaxis; thus, the pharmacist advised prescribing a proton pump inhibitor.
Duration of treatment	2	During the transition from unfractionated heparin IV infusion to rivaroxaban, heparin was discontinued prematurely	The pharmacist advised restarting the heparin IV infusion until rivaroxaban is made available and stopping heparin IV infusion at the time of administering the first dose of rivaroxaban.
Patient-transfer related	17	A patient who suffers from hypothyroidism was on levothyroxine prior to ICU admission	The pharmacist advised to restart levothyroxine 50 mcg once daily

IV intravenous; ICU intensive care unit

3.3.2.3 Monitoring need

The 'Monitoring need' category encompasses all pharmaceutical interventions related to patient monitoring, including therapeutic drug monitoring, other laboratory monitoring, and ECG monitoring. PIs within this category were mostly related to the DRP category 'Monitoring' as outlined in Table 3.10. Other PIs within this category were related to drug selection and identification of ADEs.

Table 3.10: Monitoring need category – examples and frequency

DRP category	Number of DRPs	Example of DRP	Examples of the PI category 'Monitoring need' (n=79)
Drug selection	12	The patient is on two medications that prolong the QT interval; amiodarone and fluconazole.	The pharmacist alerted about the risk of QT prolongation due to drug-drug interaction and advised ECG monitoring.
Identification of adverse effects	2	The patient was found to have dilated pupils on examination. The patient had been administered intravenous atropine for bradycardia sometime before the examination.	The pharmacist alerted that the patient had been administered atropine intravenously, which has a half-life of 3 hours and can cause pupil dilation. The pharmacist advised to keep monitoring pupils.
Monitoring	65	A patient was started on vancomycin continuous infusion after a loading dose. Due to the narrow therapeutic range, monitoring of vancomycin concentrations is required.	The pharmacist advised the need for therapeutic drug monitoring and provided instructions for the timing of vancomycin level.

3.3.2.4 Change in instructions for drug administration

Pharmaceutical interventions within this category were mostly related to the DRP category 'Drug use process', where all 58 DRPs within this category resulted in an intervention to change drug administration instruction. One intervention in this category was related to the cause of inappropriate combination of medications within the drug selection category, as described in Table 3.11.

Table 3.11: Change in instructions for drug administration – examples and frequency

DRP category	Number of DRPs	Example of DRP	Examples of the PI category 'Change in Instructions for Drug Administration' (n=59)
Drug selection	1	The patient has been taking phenytoin intravenously, which was changed to the enteral route. The patient is also on a continuous nasogastric feed. Phenytoin and the enteral feed interact, which can cause a significant drop in plasma concentration.	The pharmacist advised a change in the rate and time of enteral feed administration, allowing a 2-hour break before and a 2-hour break after administration of phenytoin via the nasogastric tube.
Drug use process	58	A patient is suffering from hypernatraemia. The patient has a significant daily intake of sodium due to multiple intravenous medications being diluted in 0.9% sodium chloride.	The pharmacist checked the compatibilities of intravenous medications currently being diluted in 0.9% sodium chloride with other diluents, 5% dextrose in this case. The pharmacist advised using 5% dextrose as a diluent (where compatible), thus minimising the intake of sodium.

3.3.2.5 Discontinue or pause medication

The pharmaceutical intervention related to discontinuation or pausing medications resulted from several DRP categories, as detailed in Table 3.12. Pharmacists mainly advised pausing medications when there was a drug-drug interaction, and one of the drugs was being used for a short course, whereas discontinuing medication was mostly suggested for cases of longer than recommended duration of treatment, inappropriate medication based on the patient's clinical status and occasions of duplication of therapy.

Table 3.12: Discontinue or pause medication category – examples and frequency

DRP category	Number of DRPs	Example of DRP	Examples of the PI category 'Discontinue or Pause Medication' (n=36)
Duration of treatment	13	A patient is on metoclopramide 10 mg three times daily, being used as a prokinetic for more than 3 days.	The pharmacist advised stopping metoclopramide after 72 hours.
Dose selection	1	A patient has been consistent on vancomycin continuous infusion for several days. Over the last 24 hours, the patient started developing an acute kidney injury. Therapeutic drug monitoring showed a supratherapeutic vancomycin concentration, showing that the dose of vancomycin is too high for the patient's renal function.	The pharmacist advised stopping the continuous infusion of vancomycin until the concentration falls into the therapeutic range.
Drug selection	19	A patient who was on simvastatin once daily has been started on clarithromycin due to community-acquired pneumonia.	Due to the drug-drug interaction between clarithromycin and simvastatin, the pharmacist advised pausing the administration of simvastatin until the patient is on clarithromycin.
Patient-transfer related	3	The patient had been admitted to the ICU with an acute kidney injury requiring dialysis. The patient's renal function was improving slowly, but the creatinine clearance was still 14 mL/minute. The patient was going to be transferred from the ICU to the general ward, and all her previous home medications have been prescribed, including metformin 500mg three times daily.	The pharmacist advised stopping metformin until the patient's renal function recovers.

3.3.2.6 Change medication

The PI category 'Change Medication' (n=19) encompassed interventions that were all related to the DRP category 'Drug Selection', however, arising from different causes within the same DRP category. An example of this intervention included the pharmacist's suggestion to change clarithromycin to doxycycline to cover atypical bacteria in a patient with community-acquired pneumonia and a prolonged QT interval of more than 500 msec. The intervention assisted in reducing the risk of developing serious arrhythmia.

3.3.2.7 Change in formulation or administration route

This category of PIs comprises all the interventions resulting from the DRP category 'Drug Form', where all DRPs classified within the Drug Form category led to a change in formulation or administration route. Additionally, two other interventions related to patient transfer also resulted to PIs requiring a change in formulation or administration route. More details and examples of interventions within this category are provided in Table 3.13.

Table 3.13: Change in formulation or administration route – examples and frequency

DRP category	Number of DRPs	Example of DRP	Examples of the PI category 'Change in formulation or administration route' (n=18)
Drug form	16	The patient was prescribed alfacalcidol capsules 1 mcg to be administered twice daily. The patient has a nasogastric tube for administering enteral medication and for feeding.	Alfacalcidol capsules cannot be opened and administered via the feeding tube. Thus, the pharmacist advised changing the formulation and using oral drops for easier administration via the nasogastric tube.
Patient-transfer related	2	The patient, who was an insulin-dependent diabetic, was prescribed a variable rate insulin infusion during the ICU stay. The patient was being transferred to a general ward, and the same insulin infusion was prescribed.	The pharmacist discussed the situation with clinicians and advised changing to a long-acting insulin injection, that was the patient's previous medication before ICU admission.

3.3.3 Pharmacological groups of medications involved in DRPs and PIs

The medications involved in identified DRPs and suggested PIs were classified on the data collection tool according to ATC code first level. Among all DRPs and PIs, anti-infectives for systemic use represented the most frequent pharmacological group, accounting for 41% (n=206) of interventions by pharmacists. Other pharmacological groups frequently involved in DRPs and PIs included medications related to the alimentary tract and metabolism (n=78 (16%)), medications used for the cardiovascular system (n=70 (14%)), medications affecting the central nervous system (n=62 (12%)) and

medications affecting blood and blood-forming organs (n=48 (10%)), as described in Figure 3.3.

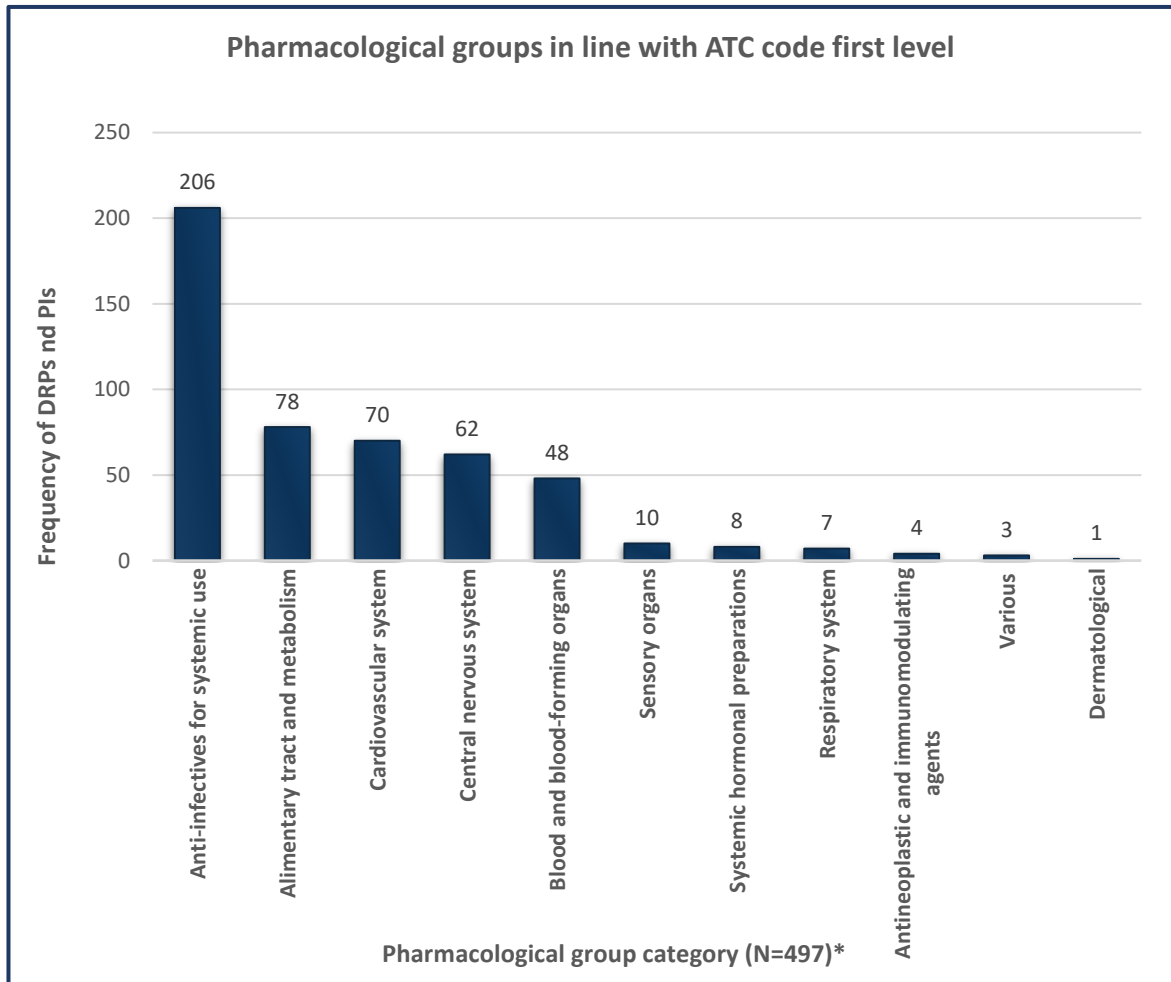


Figure 3.3: Pharmacological groups of medications involved in DRPs and PIs classified in line with ATC code first level (N=497)*

*The number of medications involved in DRPs and PIs exceeds the number of identified DRPs and suggested PIs. This arises as a result of several DRPs involving more than one group of medications, including inappropriate combinations of medications involving medications from different pharmacological groups and inappropriate parenteral drug administration method in fluid restriction or electrolyte imbalance involving more than one pharmacological group, which for this research study were classified as a single DRP.

3.3.4 Impact of pharmaceutical interventions on surrogate patient outcomes

Pharmaceutical interventions had the potential to impact surrogate patient outcomes. Pharmaceutical interventions could be related to preventing a potential adverse drug event, achieving therapeutic serum concentration of medications, assisting in fluid management, or therapeutic optimisation. All interventions recommended by pharmacists were recorded and classified on the data collection tool. One intervention could impact more than one surrogate patient outcome.

3.3.4.1 Achieving therapeutic serum concentration of medications with a narrow therapeutic range

Medications necessitating therapeutic drug monitoring (TDM) involved those with routine TDM monitoring, including the antimicrobials amikacin, gentamicin, tobramycin, and vancomycin; antiepileptics comprising sodium valproate, phenytoin, and carbamazepine; and cardiac medications such as digoxin, since the ICU caters for medical, surgical, trauma and neurological patients. Pharmacists advised on the timing for performing TDM when clinically indicated for these medications and provided interpretation of TDM results, along with subsequent dose adjustments where necessary.

There were 43 patients out of 164 patients included in the study (26%), for whom TDM was managed by pharmacists, comprising 67 TDM interventions. TDM interventions were necessary either solely for monitoring medication concentrations, due to an inappropriate combination of medications necessitating TDM, to manage drug dosing,

or because of changes in the patient’s clinical condition, for which examples are described in Table 3.14.

Table 3.14: Reasons for TDM recommendation and explanation of DRP and PI

Reason for recommending TDM	Drug-related problem	Pharmaceutical intervention
TDM recommendation arising from inappropriate combination of medications	The patient was stabilised on treatment with sodium valproate, for whom meropenem has been started due to sepsis. A drug-drug interaction between meropenem and sodium valproate can occur with the potential to decrease sodium valproate levels considerably below the therapeutic range.	The pharmacist alerted clinicians about the drug-drug interaction, with the potential of decreasing serum valproate levels. The pharmacist recommended monitoring sodium valproate concentrations. The pharmacist enquired if it is possible to change meropenem to a safer alternative antimicrobial and consider introducing another antiepileptic if drug levels are subtherapeutic and deemed necessary.
TDM recommendation due to therapy initiation of a nephrotoxic medication with a narrow therapeutic range with substantial pharmacokinetic variability	The patient had been started on gentamicin extended interval dosing. The patient was on continuous renal replacement therapy due to AKI.	The pharmacist advised TDM 8 hours post-dose since this interval is reliable due to consistent elimination through continuous renal replacement therapy. The gentamicin level was plotted on the Hartford nomogram, achieving a dosing interval of 36 hours. Thus, the same dose 36-hourly was recommended by the pharmacist until the patient was on continuous renal replacement therapy.
TDM recommendation owing to change in patient’s clinical status	The patient was stable on digoxin 0.125mg once daily from home for AF. The patient was admitted to ICU with an acute kidney injury and was oliguric.	The pharmacist advised digoxin TDM 12-24 hours following the last dose to determine whether digoxin is being eliminated. The pharmacist also advised holding the next digoxin dose until the digoxin concentration is known.

AF Atrial Fibrillation; AKI acute kidney injury; TDM therapeutic drug monitoring; ICU intensive care unit

3.3.4.2 Fluid management

The administration of intravenous fluids is necessary and frequently used in the intensive care unit. However, fluid administration has the potential to cause fluid overload.

Pharmacists intervened in minimising hidden fluids for 17 patients (10%) out of 164 patients included in the study. Fluid minimisation accounted for 19 interventions, as in most cases, a single pharmacist intervention with written instructions would be followed for the subsequent days unless there were changes in medications. Fluid minimisation was required in patients with heart failure and pulmonary oedema, patients with renal impairment who were fluid positive, patients with brain injury necessitating a neutral fluid balance, and patients with acute respiratory distress syndrome requiring a conservative fluid strategy to improve lung function.

Pharmacists suggested various recommendations related to fluid minimisation. These included concentrating infusions when administered via a central venous catheter, converting medications from IV to enteral route, and opting for a more fluid-restricted enteral feed. Examples of DRPs and PIs related to fluid minimisation are highlighted in Table 3.15.

**Table 3.15: Reasons for fluid minimisation recommendation and explanation of
DRP and PI**

Reason for recommending fluid minimisation	Drug-related problem	Pharmaceutical intervention
Patient with acute on chronic heart failure requiring minimal fluids	Several medications were being administered intravenously via peripheral venous cannula, requiring dilution in large volumes of diluents.	The pharmacist recommended minimising diluent volumes for medications that are not irritant to peripheral veins, such as piperacillin with tazobactam. Additionally, for medications that are irritant to peripheral veins, such as clarithromycin, the pharmacist suggested switching from an intravenous route to enteral administration.
Patient with traumatic brain injury, who has an overall positive fluid balance and requiring to have a neutral fluid balance	Several medications were being administered via central venous catheter contributing to extensive fluid intake.	The pharmacist suggested using minimal diluent volumes via central venous catheter for medication administration, and making use of an enteral feed that is more concentrated and requires less volume for the same daily calorific and nutritional requirements.

3.3.4.3 Prevention of a potential adverse drug event (pADE)

This expert panel assessment showed that 83.2% (n=403) of the clinical interventions suggested by pharmacists prevented some harm and had clinical relevance and were assigned a high, medium or low probability of preventing a potential ADE, whereas

25.6% (n=124) of the interventions prevented a potentially serious reaction and were assessed as having a medium probability of preventing a potential ADE. Five interventions prevented a potentially severe reaction where severe harm was potentially expected and were evaluated as having a high probability of preventing a potential ADE, and were given a pADE score of 0.6. Figure 3.4 describes how the panel of experts evaluated each intervention, while Table 3.16 presents examples of PIs along with their corresponding probability of an ADE occurring and pADE scores as assessed by the expert panel.

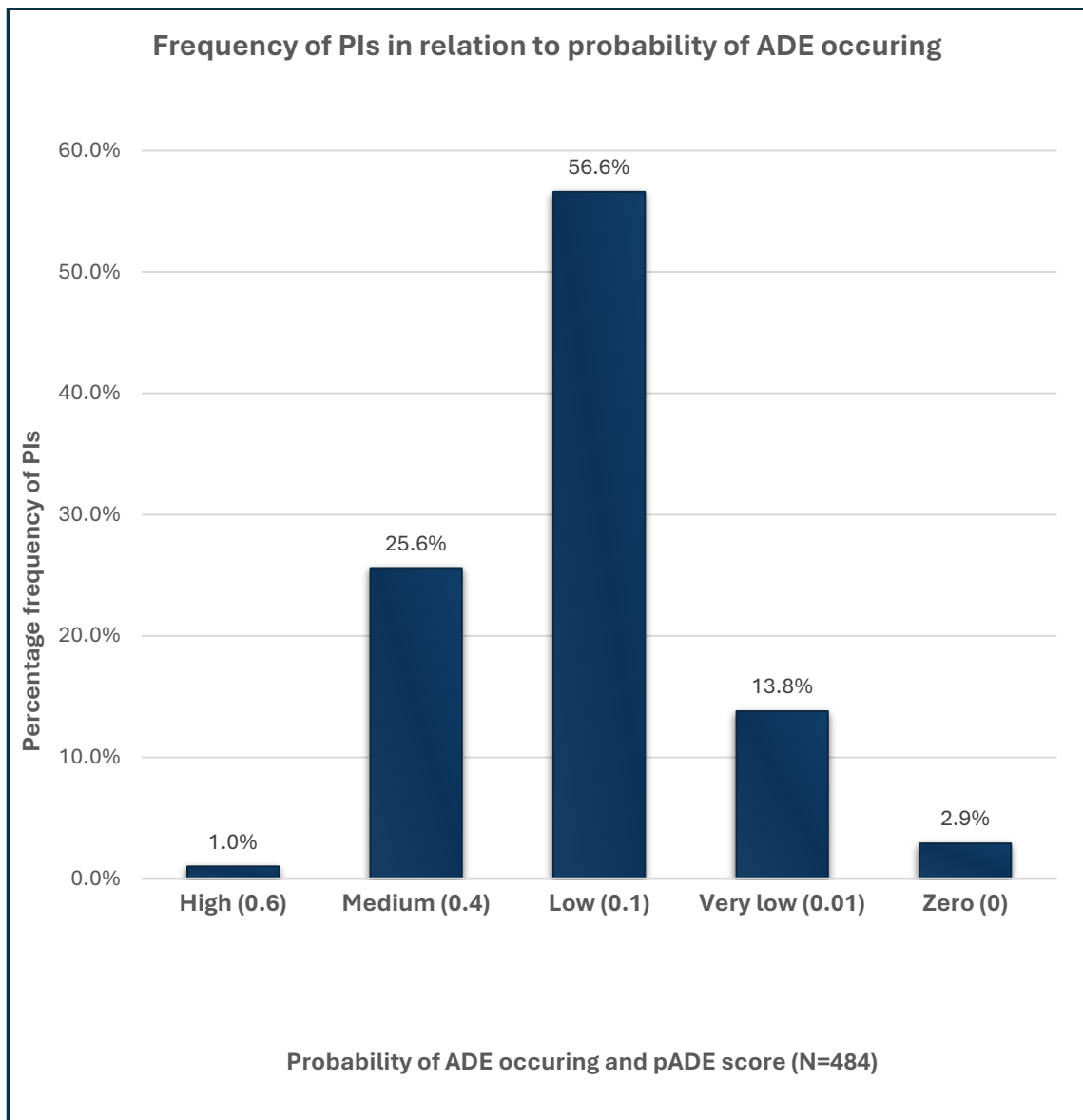


Figure 3.4: Probability of an ADE occurring and potential ADE score for pharmaceutical interventions (PIs) as evaluated by the panel of experts (N=484)

Table 3.16: Examples of PIs, assigned pADE scores and probabilities of ADE occurring using the Nesbit method⁹

Probability of ADE occurring	pADE score	Frequency (%)	Explanation of probability ^{10,11}	Examples of pharmaceutical interventions
High	0.6	5 (1.0%)	Harm is expected, life-threatening; prevented a potentially fatal or severe reaction	The pharmacist recommended stopping therapeutic heparin intravenous infusion in a patient with thrombocytopenia and a platelet count $<50 \times 10^9/L$, thus preventing a high risk of bleeding.
Medium	0.4	124 (25.6%)	Harm is expected, clinically relevant; prevented a potentially serious reaction	The pharmacist advised prescribing a variable-rate insulin infusion upon transfer of an insulin-dependent diabetic patient from the ICU to a general ward instead of subcutaneous insulin as required, thus potentially preventing severe hyperglycaemia and possibly DKA.
				The pharmacist advised stopping metoclopramide in a patient with a background of epilepsy, thus preventing a risk of seizures.
Low	0.1	274 (56.6%)	Some harm is expected, poorly clinically relevant; prevented a potentially significant reaction	The pharmacist suggested increasing the dosing interval of piperacillin and tazobactam 4.5g from 8-hourly to 12-hourly in a patient with chronic kidney disease and a creatinine clearance of 8 mL/min, thus preventing accumulation of the antimicrobial.
				The pharmacist recommended taking an amikacin trough level as TDM due to a sharp increase in creatinine to determine whether amikacin can be safely administered.
Very low	0.01	67 (13.8%)	Some harm is expected but not clinically relevant	The pharmacist advised prescribing intravenous phosphate supplementation instead of enteral supplementation in a patient with hypophosphataemia who is not tolerating enteral feed.
Zero	0	14 (2.9%)	Information only; no harm expected	The pharmacist recommended decreasing the dose of nicotine patches from 25 mg daily to 15mg daily after 8 weeks of treatment.

⁹ Nesbit TW, Shermock KM, Bobek MB, Capozzi DL, Flores PA, Leonard MC, et al. Implementation and pharmaco-economic analysis of a clinical staff pharmacist practice model. *American Journal of Health-system Pharmacy*. 2001;58(9):784–790.

¹⁰ Dong PTX, Pham VTT, Dinh CT, Le AV, Tran HTH, Nguyen HTL, et al. Implementation and Evaluation of Clinical Pharmacy Services on Improving Quality of Prescribing in Geriatric Inpatients in Vietnam: An Example in a Low-Resources Setting. *Clinical Interventions in Aging*. 2022;17:1127–1138. doi: 10.2147/CIA.S368871

¹¹ Wilkes S, Zaal RJ, Abdulla A, Hunfeld NGM. A cost-benefit analysis of hospital-wide medication reviews: a period prevalence study. *International Journal of Clinical Pharmacy*. 2022;44:138–145.

3.3.4.4 Therapeutic optimisation

Pharmaceutical interventions that had a very low or zero impact on preventing a pADE were assessed by the pharmacist researcher to determine whether they agreed with the definition of therapeutic optimisation, a proactive clinical intervention that aimed to improve patient care (Shulman et al, 2015).

All PIs classified as having very low potential for preventing a pADE (n=67) and those with zero probability of preventing a pADE (n=14) were found to be proactive pharmacist contributions aiming to enhance patient care, and thus, they were all categorised as therapeutic optimisation. Examples of such interventions are shown in Table 3.17.

Table 3.17: Examples of PIs categorised as therapeutic optimisation (n=81)

Impact of PI on Patient Outcome	Description of pharmaceutical intervention
Therapeutic optimisation	During ICU admission, the pharmacist advised prescribing brinzolamide eye drops and latanoprost eye drops since the patient suffers from glaucoma, and these were the patient's home medications and had not been restarted.
	The pharmacist advised starting lubricant eye drops in an intubated patient to prevent eye dryness.
	The pharmacist advised changing the formulation of sodium valproate from intravenously to enterally in a patient with good enteral absorption who can tolerate enteral treatment.

Chapter 4

Discussion

The aims of this research study were to develop, validate, and implement a quality system for service provision within the Intensive Care Unit and to assess the activities of clinical pharmacists in the adult Intensive Care Unit by assessing surrogate clinical outcomes. The final aim was to develop a quality measure to evaluate clinical pharmacy service provision. The significance of clinical pharmacists practising in the ICU, their role in enhancing patient outcomes and the importance of evaluation and standardisation of clinical pharmacy services were outlined in Chapter 1. This final chapter delves into the value of the results of this research, discusses the developed policy, considers the impact of pharmacist clinical interventions on surrogate patient outcomes, highlights the strengths and limitations of the study and provides recommendations for further service development and further research.

4.1 Policy development and outcomes

Policies can help define roles and responsibilities and establish a framework that ensures consistency in clinical practice. The implementation of standardisation in healthcare has demonstrated consistency in patient care and a reduction in unnecessary variation. A valuable approach to aligning pharmacists' patient care services is through the implementation of The Patient Care Process, with the ultimate objective being standardisation and reproducible patient care outcomes (Acquisto et al, 2021). In light of this, it was necessary to establish the fundamental criteria required to ensure optimal and consistent delivery of the clinical pharmacy service while taking into account the time constraints faced by the pharmacists providing the clinical service.

The Patient Care Process, with its five fundamental steps in assessing, collecting, planning, implementing, and following up on medication management while working as a member of the interdisciplinary team, was used in the developed policy for reviewing medication charts¹². Basing the medication chart review on the Patient Care Process ensures a systematic approach in collaboration with other healthcare professionals, with a focus on patient-centred care. The Standards of Practice for Clinical Pharmacists also emphasises the importance of integrating the Patient Care process with modifications, including more collaboration with the healthcare team and additional points tailored to the specific setting or patient requirements (ACCP, 2023).

One of the components that are included in the recently published Standards of Practice for Clinical Pharmacists is documentation by pharmacists in the patient's medical record, which is also encompassed in the Position Paper on Critical Care Pharmacy Services (Rudis and Brandl, 2000; Lat et al, 2020; ACCP 2023). This component was perceived as important for the local department during policy development discussions and review, and subsequently incorporated into the existing tasks performed by pharmacists practising in the ICU. Documenting specific pharmacotherapeutic recommendations in medical notes is performed in addition to verbal communication with the healthcare team, and thus, it is perceived to provide a better understanding of the pharmacist's plan regarding relevant pharmacotherapeutic suggestions.

¹² Joint Commission of Pharmacy Practitioners (JCPP). Pharmacists' Patient Care Process [online]. United States: JCPP; 2014. [cited 2023 June 24]. Available from URL: <https://jcpp.net/patient-care-process/>

Suitable documentation of pharmaceutical interventions in clinical pharmacy is important for maintaining standards of practice, improving consistency, enabling traceability, and promoting exchange of information among pharmacy staff and other healthcare professionals (Fox et al, 2011; Maes et al, 2017). By analysing trends in the documentation of clinical interventions, areas for improvement can be identified, and effective strategies can be developed. A comprehensive classification system for drug-related problems was adapted from PCNE V9.1¹³ and included in the policy for improved consistent documentation and classification of drug-related problems. The categorisation of pharmaceutical interventions was adapted to the classification of drug-related problems to document the PIs in a structured way.

The policy outlines an effective and practical approach that focuses on prioritising the tasks performed by pharmacists to deliver pharmaceutical care in the ICU. The division of pharmacists' activities into essential services and recommended activities was brought about by focusing on the core tasks for the safe provision of pharmaceutical care to patients who are critically ill. The pharmacists' activities were divided considering the needs of the local department and the time constraints faced by the pharmacists while gaining insight into the essential tasks from the Position Paper on Critical Care Pharmacy Services and the Australian Standard of practice in intensive care for pharmacy services (Rudis and Brandl, 2000; Lat et al, 2020; Johnston et al, 2021).

¹³ Pharmaceutical Care Network Europe Association (PCNE). Classification for drug-related problems V9.1 [Online]. Basel: PCNE; 2020 [cited 2023 October 26]. Available from URL: https://www.pcne.org/upload/files/417_PCNE_classification_V9-1_final.pdf

The division of pharmacists' activities into different levels of recommendations within the policy provides an opportunity and ability to monitor the level of pharmaceutical service provided on a daily basis. The policy sets the groundwork for attaining a quality measure for the clinical service provided by pharmacists in the ICU when monitoring the level of pharmaceutical service being provided. This is a continuous quality improvement strategy that involves ongoing assessment together with adjustments to improve the pharmaceutical service and process. By monitoring the level of service, one can identify an opportunity for growth of the service.

4.2 Impact of the drug-related problems and the pharmaceutical interventions identified

Study design and process variations can inhibit exact comparisons with other research related to clinical pharmacist activity in the intensive care unit. However, when compared to other studies relating to pharmaceutical interventions in the ICU, certain similar trends may be observed. In the current study, 'antimicrobials for systemic use' was the therapeutic class most frequently involved in DRPs and PIs, accounting for 41% of the cases. This finding compares with other studies related to pharmaceutical interventions in the ICU, showing a similar relationship with antimicrobials (Klopotowska et al, 2010; Martins et al, 2019; Cviki and Sinkovic, 2020; Chiang et al, 2021; Houso et al, 2022). The frequent occurrence of suspected or proven infections in critically ill

patients, as reported by Vincent et al (2020), likely contributes to the high number of PIs related to antimicrobials for systemic use.

The most frequent DRP identified by the pharmacists was 'Dose Selection', where 38% of the DRPs fell in this category. These DRPs resulted in 40% of the pharmaceutical interventions involving dose adjustments, which were mostly related to adjusting medication doses due to renal function, liver function, body weight, severity of infection, drug-drug interactions, adverse effects due to specific medications, and renal replacement therapies. Similar trends of DRPs related to the adjustment of doses or dosing intervals were observed in studies relating to pharmaceutical interventions in the ICU (Richter et al, 2016; Cviki and Sinkovic, 2020; Chiang et al, 2021). While overdosing increases the risk of adverse drug events, underdosing may lead to therapeutic failure. Consequently, achieving optimal dosing in patients with changing clinical conditions in intensive care may necessitate frequent dose adjustments.

The pharmacists also identified DRPs associated with the 'Drug Selection' category, which constituted the second most frequent category, accounting for 24% of all DRPs. Such DRPs resulted in pharmaceutical interventions mostly related to the addition of a medication, discontinuation or pausing a medication, changing medication, or monitoring. A recent research study carried out by Rayner (2021) in the local setting captured pharmaceutical care issues carried out by one pharmacist and had somewhat similar results. The most frequent categories of DRPs identified by Rayner (2021) were 'Drug Selection' (44%), followed by 'Dose Selection' (19.6%), the same two most

frequent categories identified in the current study. However, the pharmacists identified more DRPs related to 'Dose Selection' (38%) in the present study. This change could be attributed to the fact that in the research by Rayner (2021), the service was new at the time of the study, whereas currently, the team of pharmacists are more experienced and delve deeper into pharmacokinetic and pharmacodynamic alterations which require medication dose adjustments.

'Monitoring' was the next frequent DRP category identified by pharmacists, where 13% of all DRPs were related to this category. Pharmaceutical interventions related to monitoring need amounted to 16% of all interventions recommended by pharmacists and arose due to monitoring, drug selection and identifications of adverse events. Monitoring could be related to TDM, other laboratory monitoring, such as creatine kinase levels in patients on daptomycin or other patient monitoring, such as ECG monitoring in patients who are being administered medications that prolong the QT interval. Other studies have reported varying degrees of DRPs related to monitoring; Cvikl and Sinkovic (2020) found an 18% incidence, while Martins et al (2019) reported an 8% occurrence.

4.3 Assessing the impact of pharmaceutical interventions on surrogate patient

outcomes

Studies have shown that pharmacists practising in the ICU can contribute to improving medication safety and patient outcomes by being members of the ICU interdisciplinary

team and providing pharmacist-managed medication changes (Kane et al, 2003; Shulman et al, 2015; Bauer and Kane-Gill, 2016; Lee et al, 2019). Contributions of clinical pharmacists practising in the ICU in Malta were categorised according to their impact on surrogate patient outcomes and assessed by an expert panel.

Surrogate clinical endpoints, such as achieving therapeutic serum concentrations, have been investigated for critically ill patients (Kane et al, 2003). Personalised therapeutic drug monitoring improves consistency in maintaining appropriate therapeutic ranges of medications.

In the local ICU, TDM is mainly managed by pharmacists, where pharmacists provide instructions on the necessary TDM and proper timings for measuring medication concentrations. In the current study, 26% of the patients required TDM, which was managed by the pharmacy team. The ICU serves a mixed population of medical, surgical and neurocritical patients, requiring TDM not only for antimicrobials but also for anti-epileptic medications. The varied patient population in our ICU and the fact that pharmacists are present in the ICU seven days a week, may explain the number of patients requiring TDM in this study. Bourne et al (2014) reported a higher proportion of TDM interventions by pharmacists in a neurocritical care unit when compared with a general ICU.

Clinical interventions related to TDM were recommended due to several factors, including changes in the patient's clinical condition, the introduction of an interacting

medication, a change in renal replacement therapy, and starting medication with a narrow therapeutic range in critically ill patients with varying pharmacokinetics. Results of TDM helped achieve concentrations within the therapeutic range, thus avoiding subtherapeutic concentrations that may lead to therapeutic failure and preventing supratherapeutic medication concentrations that may lead to toxicity. Pharmacists provided guidance on dose adjustments, including those related to vancomycin, as well as dosing interval adjustments for aminoglycosides using extended interval dosing. In specific cases, pharmacists also advised omitting the dosing of a medication until the concentration fell within the therapeutic range, particularly in cases where patients had a sudden deterioration in renal function. Streetman et al (2001) reported a significant overall reduction in the frequency of nephrotoxicity with aminoglycosides when individualised pharmacokinetic monitoring was employed. Similarly, TDM-guided dosing for vancomycin lowered the risk of nephrotoxicity and significantly improved clinical cure rates in patients treated with vancomycin (Ye et al, 2013).

Overall, pharmacists can assist in achieving clinical endpoints by monitoring medication concentrations (Arredondo et al, 2021). Pharmacist-led TDM in the current research study helped to guide the ICU team in adjusting drug dosing as necessary to maintain drug concentrations within the recommended therapeutic range. Furthermore, TDM to balance efficacy and toxicity is one of the reasons for which a pharmacist is recommended in the ICU, as described in a recent article by McKenzie et al (2024).

Another surrogate clinical outcome that has been investigated for critical care patients is fluid management (Kane et al, 2003). Gamble et al (2022) reported that the amount of fluid intake in critically ill patients via hidden fluids in the first three days of ICU admission is around 40% of the total fluid intake. Administration of significant volumes of hidden fluids can lead to fluid overload (Branan et al, 2020).

During the current study, the pharmacists advised fluid minimisation in 17 patients (10% of the total number of patients) by instructing a reduction in the volumes of hidden fluids being administered. Several patient conditions and comorbidities necessitated fluid minimisation or fluid restriction. One pharmaceutical intervention related to hidden fluids for a patient with acute on chronic heart failure resulted in a reduction of 700 mL of hidden fluid intake over 24 hours. Another case involved a patient with a brain injury requiring a neutral fluid balance, where the pharmacist suggested minimising hidden fluids, resulting in a reduction of 820 mL over 24 hours, which previously contributed to a positive fluid balance.

The pharmacists mainly used three approaches for minimising the intake of hidden fluids, namely utilising more concentrated intravenous administrations via central venous catheter, using a higher calorie and higher protein enteral feed where appropriate, and changing intravenous medications to enterally where appropriate, essentially when they were administered via peripheral venous catheter and could not use a more concentrated solution. The pharmacist's role in fluid stewardship has been described in a report by Hawkins et al (2022). Though the study focuses on wider fluid

stewardship recommendations including the administration of fluid boluses and maintenance fluid, the recommendations for fluid stewardship for hidden fluids and targeted fluid minimisation strategies are similar to what the pharmacists recommended in the current study. Considering that particular patients might be more susceptible to complications of fluid therapy and that hidden fluid volumes contribute a significant amount of fluid intake, pharmacist recommendations to minimise hidden fluids are significant and can help mitigate fluid overload.

Expert panel evaluation of all PIs carried out by pharmacists during the study period showed that the majority of clinical interventions (84%) prevented a potentially significant reaction, were clinically relevant and had a low, medium or high probability of preventing a pADE. Similarly, Bosma et al (2018a), in an intervention study related to pharmaceutical interventions in two ICUs in the Netherlands, reported approximately 70% of interventions with a low probability and approximately 10% of interventions with a medium probability of preventing a pADE when using the Nesbit method (Nesbit et al, 2001). The interventions were assessed by an expert panel of healthcare professionals made up of an intensivist and a hospital pharmacist with ICU experience, which is comparable to the current study. Other studies were carried out in different settings, and thus, a direct comparison cannot be carried out. However, in a study by Gallagher et al (2014), in a hospital-wide study in Ireland, 3% of interventions were found to have a high, 26% medium, and 36% low probability of preventing a pADE when using the Nesbit method and evaluated by an expert panel made up of two academic pharmacists

with hospital pharmacy experience (Nesbit et al, 2001). Differences in setting and expert panel composition could lead to different results.

During the present research study, approximately one-fourth of all interventions (26%) prevented clinically relevant harm and potentially serious reactions and had at least a medium probability of preventing a pADE. These categories of PIs included dose adjustment or dosing interval adjustment of nephrotoxic medications, stopping medications which could be contraindicated in specific patients, changing medications in view of interactions resulting in QT interval prolongation, minimising fluids in fluid-restricted patients, and interventions related to insulin in insulin-dependent diabetic patients. Similarly, the monitoring of ECG for QT interval prolongation due to multiple medications known to prolong the QT interval is also described by Bosma et al (2018a), where a particular intervention based on four medications which prolong the QT interval was given a score of 'potentially lethal' using a different scoring system.

In the current study, five interventions were evaluated as highly likely to prevent a pADE in the absence of the PI. Four of these interventions were related to anticoagulants, which are high-risk medications. All four interventions prevented a bleeding risk. Two of the interventions were related to using a direct oral anticoagulant or low molecular weight heparin in two separate patients with acute kidney injury. The panel of experts agreed that the risk of bleeding in critically ill patients was high had the intervention not been carried out. Similarly, Kearney et al (2017) and Ronan et al (2020), although their studies were conducted in different settings, reported a high probability of a pADE

associated with anticoagulants. Specifically, the DRP was related to the duplication of prescriptions for anticoagulants within the same therapeutic class.

An exact interpretation of the definition of an ADE would exclude the omission of medications from being included as potentially preventing an ADE since the medication was not administered, and an ADE directly related to the medication could not have happened (Bates et al, 1995; Gandhi et al, 2000). However, omission of medications was included in this research study since not receiving a particular medication may increase the risk of patient harm, and similarly, this category of drug-related problems was included in previous studies assessing the potential prevention of ADEs (Gallagher et al, 2014; Bosma et al, 2018b; Ronan et al, 2020; Dong et al, 2022; Wilkes et al, 2022). Moreover, medication omissions and other medication discrepancies have been described as potential ADEs (Kripalani et al, 2012).

In this research study, the focus was on evaluating clinical interventions that could prevent potential ADEs. This study did not specifically assess the value added of interventions that aimed at improving the efficacy of medication therapy. Nevertheless, it is plausible that such interventions may contribute significantly to patient care. The provision of antimicrobial prophylaxis managed by pharmacists was linked to significant improvement in both clinical and economic outcomes for patients in need of surgical antibiotic prophylaxis (Bond and Raehl, 2007), while anticoagulation services led by pharmacists in hospitals appeared to improve the quality of patient care (Lee et al, 2016). Moreover, Bosma et al (2018a) evaluated all pharmaceutical interventions in the

ICU for the value of service using a validated and published tool, resulting in the majority of interventions (>70%) having a significant value.

4.4 Strengths and limitations

This research study was a quality evaluation study involving a substantial number of patients and interventions, contributing to reliable results. The pharmacist researcher included all interventions carried out by a team of pharmacists, thus mitigating potential bias. The study has several strengths, namely the robust assessment of pharmaceutical interventions by an independent expert panel unrelated to the study, consisting of multidisciplinary expertise and the use of a validated tool to evaluate the interventions. The developed policy was thoroughly reviewed by both internal validators and healthcare professionals external to the pharmacy directorate, enhancing its overall reliability.

Limitations of the study include the research being conducted in one ICU only, which may limit the generalisability of findings. Although a team of pharmacists attend the ICU ward rounds on a daily basis, the time spent in the ICU is still limited. The pharmaceutical interventions carried out were extracted from an online patient profile, which could potentially have resulted in underreported or insufficiently explained interventions, which could, in turn, have affected their accurate evaluation. The inclusion of a pharmacist on the expert panel assessing the interventions who was also involved in providing ICU clinical pharmacy services can lead to bias. Nonetheless, it was logical to

include a pharmacist with ICU experience on the expert panel, and currently, the only pharmacists with ICU experience are the ones currently providing the clinical pharmacy service.

4.5 Recommendations

During this research study, a number of recommendations related to service development and research development were identified.

4.5.1 Recommendations for service development

The developed policy has led to the identification of the necessary standard operating procedures (SOPs) that pertain to the tasks performed by pharmacists in the ICU. Service development could focus more on those recommended activities, such as treatment chart reviews for patients being transferred out of ICU, to be included as essential in the future since this activity is also susceptible to errors and potential ADEs, as shown by Bosma et al (2018b). Additionally, the current model of clinical pharmacists working in the ICU can be extended to other critical areas in the hospital. More service development should be related to additional pharmacy guidelines to be used in the ICU, such as a vancomycin continuous infusion guideline and guidelines for the dose adjustment of antimicrobials to be used with sustained low-efficiency dialysis (SLED), a novel method of dialysis in our unit.

4.5.2 Recommendations for further research

This research project provides a foundation for the quality evaluation of clinical pharmacy services across other hospital clinical areas. The developed policy lays the groundwork for a quality metric to measure the outcomes of clinical pharmacy service provision, enabling service evaluation.

Moreover, further research could aim for a cost-benefit analysis of clinical pharmacy interventions. Studies have already been carried out investigating cost-benefit analysis using the Nesbit method (Nesbit et al, 2001; Wilkes et al, 2021; Houso et al, 2022).

Once the pharmacist's review of the treatment chart during the transition becomes an essential part of the ICU practice, an evaluation of PIs related to the area can be performed, following a similar approach to Bosma et al (2018b). During this research study, a number of interventions related to patient transfer were already identified, indicating the need for further research in this intervention category.

Further research could explore identifying patients who are at higher risk of ADEs, which could be due to several factors such as clinical condition, comorbidities, the total number of medications being used, or the specific use of high-risk medications. It would be of interest to identify more at-risk patients so that pharmacists can allocate the necessary time, particularly when time constraints are a concern. During a recent multicentre study in the United States by Sikora et al (2022), a tool for medication

complexity was investigated for its ability to anticipate patient outcomes in the ICU together with the quantity and quality of pharmacist intervention. The tool is based on medication and patient complexity and quantifies the complexity of a patient's medication regimen in the ICU. Further research could also investigate the use of a medication complexity tool.

4.6 Conclusion

The study aids in establishing standardised practices for clinical pharmacists within the ICU, ensuring consistency in the quality of service in this area. The robust policy provides a comprehensive overview of the activities of the pharmacists practising in the ICU, their interactions with the interdisciplinary ICU team, and their collective effort to optimise patient safety and improve patient outcomes. Working in line with the developed pharmacy policy ensures a consistent quality of service on a daily basis.

This study demonstrates that pharmacists' interventions in the ICU are effective in optimising surrogate patient outcomes when integrated into an interdisciplinary team. The results highlight the effectiveness of pharmacists' interventions in the ICU in reducing the risk of occurrence of pADEs. Whilst the risk impact was estimated to range between high to very low, a key aspect of patient-centric care is providing optimised pharmacotherapy to mitigate individual patient risks as a result of medication use. The significant proportion of interventions evaluated as medium or high, likely preventing at

least a potentially serious reaction, highlights the critical role of pharmacists in the ICU as part of the interdisciplinary team.

The overall findings of the study suggest that the clinical pharmacy service currently being provided in the local ICU is effective in enhancing overall patient safety and can be applied to other critical areas in the hospital. Furthermore, this study contributes to the body of evidence supporting the significance of pharmacists' interventions in the ICU especially in optimising pharmacotherapy to reduce patient risks.

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Appendix 1

University Research Ethics Committee Approval



**L-Università
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Ref No: MED-2023-00216

12 September 2023

Ms Ruth Agius
10, Triq il-Pensjeri,
Santa Luċija
SLC 1750

With reference to your application submitted to the Faculty Research Ethics Committee in connection with your research entitled:

Quality Evaluation of Clinical Pharmacy Services in an Intensive Care Unit (ICU)

The Faculty Research Ethics Committee is granting ethical approval for the above-mentioned application.

Professor Anthony Serracino Inglott
Chair
Faculty Research Ethics Committee

Appendix 2

Policy for Clinical Pharmacy Service Provision within the Intensive Care Unit

**Policy for Clinical Pharmacy Services Provision within the
Intensive Care Unit**

Version Number	1.1	
Policy Owner	Pharmacy Directorate Intensive Care Unit (Intensive Therapy Unit)	
Author	Ruth Agius	
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1. POLICY STATEMENT

This policy describes the various responsibilities of pharmacists in the Intensive Care Unit (ICU), who are part of the interdisciplinary team and are involved in direct and indirect patient care.

The purpose of this policy is to define and standardise the activities of pharmacists providing a clinical pharmacy service in the ICU, in line with Mater Dei Hospital (MDH) Intensive Therapy Unit Operational Policy, to provide optimal care to ICU patients.

2. RATIONALE

Due to the recently introduced clinical pharmacy services within the ICU, a policy is required to consolidate pharmacists' service provision within the ICU, enhancing consistency and ensuring standardisation. The clinical pharmacy service evolves around activities related to direct patient care and those related to indirect patient care.

2.1 Direct patient care

Clinical pharmacy service provision within the ICU environment and during ICU interdisciplinary ward rounds aims at delivering pharmaceutical care, which is definable as 'the pharmacist's contribution to the care of individuals to optimise medication use and improve health outcomes'¹. This involves working closely with other healthcare professionals to best contribute to the patient's management. The pharmacist reviews medication charts and provides the necessary medicine information to healthcare professionals at the bedside, thus, optimising medication use in the ICU.

2.2 Indirect patient care

Pharmacists have a role in implementing quality improvement initiatives and protocols within the ICU. Pharmacists contribute to the development and update of guidelines and drug monographs specifically for ICU use through a systematic approach. Pharmacists are also involved in reporting adverse drug reactions (ADRs) to relevant authorities and reporting safety issues via the safety alert system for learning at MDH.

3. APPLICABILITY

This policy applies to pharmacists involved in providing clinical pharmacy services within the ICU at Mater Dei Hospital.

For the intent and purpose of this policy:

- The term ICU (ITU) refers to the Intensive Care Unit (Intensive Therapy Unit) at Mater Dei Hospital.
- The term pharmacist refers to pharmacists working within the ICU environment directly with clinicians, other healthcare professionals and patients, ensuring that prescribed medications contribute to the best possible outcomes⁴.
- iSoft Clinical Manager (iCM) is electronic software used by the hospital to record all laboratory investigation results, radiology reports, and Accident and Emergency admission notes, which helps support clinical decisions.
- Prescription, Administration and Monitoring (PAM) chart is a document available at Mater Dei Hospital to prescribe, monitor and adjust doses of medications with regular laboratory monitoring or therapeutic drug monitoring. The medications requiring a PAM chart are Heparin intravenous infusion, Vancomycin, Amikacin, Gentamicin and Tobramycin.
- The Pharmacy Patient Profile is an individual patient record filled in by the pharmacist upon patient admission and updated daily. It is a tool used by pharmacists to provide all patient details and daily updates. The patient profile includes patient demographics, reason for admission to ICU, past medical history, medication history, allergies, medication therapy at ICU (current medication and medication which has been stopped), active problems, pertinent laboratory investigations, drug-related problems, therapy modifications, and pharmaceutical interventions.

4. ROLES AND RESPONSIBILITIES

4.1 Pharmacists working within ICU²

- Prepare for the morning ward round by identifying newly admitted patients and reviewing and recording pertinent laboratory blood results of all patients
- Attend morning ward rounds in the ICU as a member of the interdisciplinary team providing pharmaceutical care to patients admitted to the ICU and clinical support to the ICU team
- Review medication therapy for appropriate indication, dose, dosage regimen, drug interactions, drug allergies and duplication of therapy, and advise as necessary
- Perform repeated reviews of medication charts during the ICU stay due to changes in patients' clinical condition and frequent medication changes
- Review medication history to determine which medications should be continued and which should be stopped during the ICU admission
- Collaborate and communicate effectively with other healthcare professionals to optimise patient care
- Advise about therapeutic drug monitoring and subsequent dose adjustments
- Provide drug information, administration instructions, and intravenous compatibility information to the ICU team
- Participate and assist in reporting relevant ADRs to the Malta Medicines Authority through MDH Pharmacy Quality Team
- Identify and assist in the prevention and management of adverse drug events
- Report patient-related safety issues through the Safety Alert System for Learning
- Document all clinical activities and pharmaceutical interventions in the electronic pharmacy database by categorising and quantifying interventions carried out by pharmacists
- Contribute to the development and update of clinical guidelines, protocols and policies related to medication use in the ICU
- Develop and update ICU-specific drug monographs
- Provide support through liaison with various pharmaceutical departments on drug

availability, licensing issues, and other pharmaceutical matters

- Provide guidance with respect to prescribing within the government hospital formulary
- Discuss any pertinent drug therapy issues with pharmacy management.

4.2 MDH Pharmacy – Clinical Pharmacy Services

Provision of clinical pharmacy services for ICU on a daily basis.

4.3 Interdisciplinary ICU Team

Pharmacists work as part of the interdisciplinary ICU team. Healthcare professionals need to receive adequate information for optimal decision-making. Medication-related input from pharmacists is essential.

5. FUNCTIONS

5.1 Updating patient profiles prior to ward round

- Pharmacy patient profiles are updated daily before the morning ward round.
- New patient profiles are created for newly admitted patients to ICU. Patient profiles include patient details, admission information (if available on iCM), medical history and medication history (if available on iCM), pertinent laboratory blood investigations, and other relevant investigations.
- Patient profiles for patients still admitted to the ICU are updated with the new laboratory blood investigations from iCM over the last 24 hours.
- All profiles of patients in ICU are made available for the pharmacists during ICU ward rounds for ease of reference and for timely updates on patient clinical progress, medication changes, and pharmaceutical interventions.

5.2 Daily participation in morning ward rounds and/or medication chart review

The pharmacists work as part of the interdisciplinary healthcare team in the ICU. The pharmacists use a consistent process that aligns with the main components of the Pharmacists' Patient Care Process^{3,4}. This process is built on a patient-centred care approach, close collaboration with the healthcare team, effective communication, and good documentation of the services provided. The Pharmacists' Patient Care Process provides a consistent, stepwise approach for services delivered by pharmacists and consists of five steps; collect, assess, plan, implement, and follow-up³.

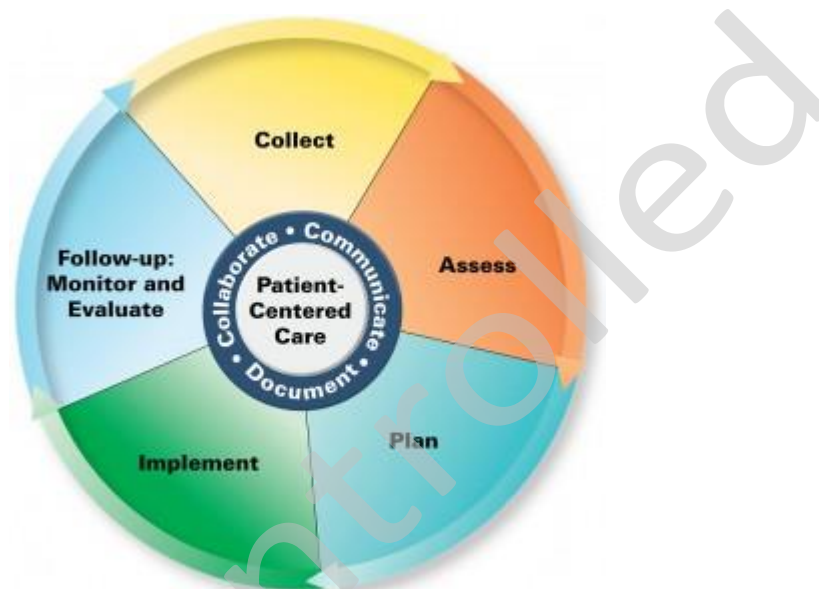


Figure 1: The Pharmacists' Patient Care Process³

5.2.1 Medication chart review

During or prior to the morning ward round, the pharmacists review patients' medication charts, collect and analyse information and develop a pharmaceutical care plan by:

- a. **Collecting** the essential subjective and objective information about the patient to understand the important medical history, medication history and current clinical status of the patient.
 - Collect relevant medical history and medication history from reliable sources.

- Collect information about the patient's current clinical status through a system-based approach. Obtaining this information is a crucial step in patient assessment in the ICU since patients are critically ill, pharmacokinetics are altered, and any changes to medications should be based on the patient's current clinical condition.
- b. **Assessing** the collected information and analysing the clinical effects of the patient's medication therapy in the context of the patient's clinical condition to identify and prioritise problems with medication use to achieve optimal care. Examples of this process may include:
- Assessing medications on the treatment chart for appropriateness, effectiveness, and safety. The pharmacist ensures that the medication, dose, frequency of administration, and administration times for each medication are clear, complete, and correct.
 - Assessing dilutions, concentrations and rates of infusion of medications being given via infusion
 - Assessing Prescription, Administration and Monitoring (PAM) Chart
 - Assessing the need for therapeutic drug monitoring for medications with a narrow therapeutic range whose levels are processed locally
 - Assessing for drug-drug interactions, drug-feed interactions and required monitoring
 - Assessing the patient's clinical status and contraindications related to the use and administration of medications
 - Assessing which medications from the medication history need to be continued in ICU and those which need to be stopped
 - Assessing treatment charts for clarity and completeness, duplication of therapy and medication administration corresponding to prescription
- c. **Developing** a pharmaceutical care plan in collaboration with other healthcare professionals. The pharmaceutical care plan addresses medication-related problems, optimises medication therapy in keeping with the clinical status of the patient and contributes to the goals of therapy. The process may include:

- Need for a dose modification
 - Need for introduction of a new medication
 - Need for stopping or pausing a medication
 - Need for change of medication
 - Need for change of formulation or change in administration route
 - Need to include or change drug administration instructions
 - Need for therapeutic drug monitoring and other patient or laboratory monitoring
- d. **Implementing** the pharmaceutical care plan in collaboration with other healthcare professionals. During the process, the pharmacist
- Addresses medication-related problems and suggests pharmaceutical interventions to optimise treatment, in discussion with ICU healthcare professionals. Pharmaceutical interventions are in line with the process in section 5.2.1(c) above and are verbally communicated to the ICU team.
 - Provides guidance to other healthcare professionals about treatment administration and monitoring, including therapeutic drug monitoring. Pharmacists advise healthcare professionals about therapeutic drug monitoring, providing clear instructions related to the timing of serum levels and subsequent advice on dose adjustments or changes in dosing intervals.
- e. **Monitoring and evaluating** the effectiveness of the pharmaceutical care plan and discussing alterations of the plan together with other healthcare professionals. This process includes the continuous monitoring and assessment of medication appropriateness, effectiveness, and safety through daily review of the medication charts.

5.3 Provision of medicine information and administration instructions to healthcare professionals in the ICU

- The pharmacists provide patient-specific medicine information to ICU healthcare professionals to guide medication therapy decisions.
- Pharmacists advise about instructions for the compatibility and administration of specific parenteral and enteral medications according to the patient's particular needs.

5.4 Liaison with pharmaceutical departments concerning matters directly related to patient care

Pharmacists practising in ICU liaise with ICU healthcare professionals, other MDH pharmacists, and pharmaceutical departments as necessary for drug availability issues, licensing issues, formulary management, and other pharmaceutical matters directly related to patient care.

5.5 Medication chart review for patients transitioning out of ICU

Patients may be transferred from ICU to a general hospital ward at any time of day. When patients are transferred out of the ICU during the time when pharmacists are present, pharmacists review the treatment chart before ward transfer as part of medication reconciliation.

5.6 Update of patient profiles following ward round

- After the ward round, all patient profiles are updated with changes to treatment, reasons for treatment modifications, pharmaceutical interventions, major changes in clinical condition, and other important issues. New regular treatment is included, and treatment that has been stopped is crossed out.
- Patient profiles should be as complete and accurate as possible, both for use by

other pharmacists and for future reference.

- Pharmaceutical interventions that need follow-up are specified as such in the patient profile to be followed up the next day by the pharmacist on duty.

5.7 Documentation of specific pharmacotherapeutic recommendations in the patient's medical notes

Pharmacists may make use of medical notes to document specific pharmacotherapeutic recommendations, which may arise in response to a recognised pharmacotherapeutic consult such as antibiotic therapeutic drug monitoring. Medical notes complement verbal communication with the entire patient care team.

5.8 Documentation of clinical activities and pharmaceutical interventions

By documenting clinical pharmaceutical interventions in a standardised manner, pharmacists can record all the work carried out. All accepted pharmaceutical interventions are documented in the electronic database on SharePoint. Categories and descriptions for drug-related problems and pharmaceutical interventions are described in Appendix 2. Pharmaceutical interventions and clinical activities that need to be followed up are recorded in the pharmacy patient profile to be completed the following day.

5.9 Reporting Patient Safety Events

Patient safety event reporting supports the detection of patient safety incidents and quality problems within hospitals. This system relies on voluntary reports submitted by healthcare professionals providing detailed information about patient safety events.

Patient safety issues are reported via an electronic system to the SA Learn Team (Safety Alert System for Learning) with the intention of enhancing patient safety and improving quality of care and preventing avoidable harm.

5.10 Reporting Adverse Drug Reactions (ADRs)

ADR reporting is a critical component of proactive patient safety allowing healthcare systems to continuously improve and provide safer care.

When an ADR is suspected, pharmacists assist in investigating the suspected ADR and in providing patient care. Suspected ADRs are discussed with the caring consultant or delegate. Pharmacists practising within the ICU take an active role in reporting the suspected ADR by informing the Quality Team within the Pharmacy Directorate to analyse the ADR and understand its cause. Subsequently, the ADR is reported to the Malta Medicines Authority via the online Adverse Drug Reaction and Medication Error Report Form. Detailed documentation of the ADR is essential to ensure safety trends are monitored.

5.11 Development and update of guidelines and monographs

As members of the interdisciplinary team, the pharmacists contribute to the development and update of clinical guidelines and protocols related to medication use in the ICU. The pharmacists carry out the necessary research to stay abreast with current evidence related to the guidelines and assist in the development or revision of these guidelines. Additionally, pharmacists contribute towards the implementation of these guidelines.

Pharmacists are also responsible for developing and updating ICU-specific drug monographs, which serve as an essential reference for medications used in the ICU. The pharmacists utilise available resources and updated literature and are conversant with current practices in the ICU.

All clinical guidelines, protocols, and monographs involve a systematic process where two pharmacists perform independent verification to ensure the quality and reliability of the system.

5.12 Prioritising functions carried out by pharmacists in ICU

Pharmacists working in the ICU perform tasks that can be categorised as either direct patient care or indirect patient care, as outlined in Section 2 above.

These functions have been further divided into two categories, as described in Table 1:

- **Essential activities:**
 - Direct patient care activities that are crucial for ensuring the safe provision of pharmaceutical care to critically ill patients,
 - Indirect patient care activities that are fundamental for the safe continuity of the clinical pharmacy service
- **Recommended activities:**
 - Direct patient care activities that are desirable within the ICU environment and are carried out in addition to the essential activities directly related to patient care
 - Indirect patient care activities that are necessary for maintaining the continuity of the clinical pharmacy services and are carried out in addition to all other essential and recommended activities

Table 1: Essential and recommended activities of pharmacists in ICU

Direct patient Care		Indirect Patient Care	
Essential Activities	Recommended Activities	Essential Activities	Recommended Activities
Participation in daily morning ward rounds and/or medication chart review	Updating patient profiles prior to ward round	Reporting Patient Safety Events	Documentation of clinical activities and pharmaceutical interventions
Provision of medicine information and administration instructions to healthcare professionals in the ICU	Medication chart review for patients transitioning out of ICU	Reporting Adverse Drug Reactions (ADRs)	Development and update of guidelines and ICU-specific monographs
Liaison with pharmaceutical departments concerning matters directly related to patient care	Documentation of specific pharmacotherapeutic recommendations in the patient's medical notes		
Update of patient profiles following ward round			

6 POLICY PROVISIONS

Contents of this policy will be made known to Mater Dei Hospital.

Any breaches of the policy by MDH staff will be channelled through their line managers, where the latter will take forward any required corrective and preventive actions (CAPA).

Any document issued de novo in relation to the subject matter covered within this policy is to be in line with the same. Documents that are already in force should be updated accordingly.

7 REFERENCE TO OTHER MDH DOCUMENTS

- MDH Intensive Therapy Unit Operational Policy

8 SOURCE REFERENCES AND ACKNOWLEDGEMENTS

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2. Rudis MI, Brandl KM. Position paper on critical care pharmacy services. *Critical care medicine*. 2000 Nov 01;28(11):3746-3750.
3. Joint Commission of Pharmacy Practitioners (JCPP). Pharmacists' Patient Care Process [online]. United States: JCPP; 2014. [cited 2023 October 24]. Available from URL: <https://jcphp.net/patient-care-process/>
4. American College of Clinical Pharmacy. Standards of practice for clinical pharmacists. *Journal of the American College of Clinical Pharmacy*. 2023;6(10):1156-1159.
5. Pharmaceutical Care Network Europe Association (PCNE). Classification for drug-related problems V9.1 [Online]. Basel: PCNE; 2020 [cited 2023 October 26]. Available from URL: https://www.pcne.org/upload/files/417_PCNE_classification_V9-1_final.pdf

Appendix 1: Patient Profile for ICU Clinical Pharmacy Services

Bed no.	Name	Age (years)	Actuals Weight (kg) Ideal body weight (kg)	Height (cm)
Diagnosis/ Reason for Admission to ICU:				
Past Medical History:				
Medication History (pre-admission to ITU/hospital)				
Allergies:				
Current treatment: Antimicrobials: Continuous infusions: Discontinued medications:				
Pharmacist notes:				
Date:	Laboratory investigations:			
	Current problems, therapy modifications, pharmaceutical interventions:			
Date:	Laboratory investigations:			
	Current problems, therapy modifications, pharmaceutical interventions:			
Date:	Laboratory investigations:			
	Current problems, therapy modifications, pharmaceutical interventions:			

Appendix 2: Description of drug-related problems and pharmaceutical interventions

Description of drug-related problems

Drug-related problem ⁵	Description
Drug selection	Inappropriate medication according to guidelines/formulary No indication for drug Inappropriate combination of medications - drug interaction Inappropriate duplication of therapeutic group or active ingredient No or incomplete drug treatment despite existing indication Too many drugs/ active ingredients prescribed for indication Inappropriate medication based on the patient's clinical status
Drug Formulation	Inappropriate drug formulation for this patient Another drug formulation or route of administration more appropriate for this patient
Dose selection	Dose too low Dose of single active ingredient too high Dosage regimen not frequent enough Dosage regimen too frequent Dose timing instructions wrong, unclear, or missing
Duration of treatment	Duration of treatment too short Duration of treatment too long
Dispensing	Prescribed medication not available Wrong drug or strength made available at ward
Drug use process or drug administration	Inappropriate timing of administration or dosing intervals by a healthcare professional Drug under-administered by a healthcare professional Drug over-administered by a healthcare professional Drug not administered at all by a healthcare professional Wrong drug administered by a healthcare professional Drug administered via the wrong route by a healthcare professional Inappropriate parenteral/enteral drug administration method
Patient-related	Patient physically unable to use drug/form as directed
Patient transfer related	Medication reconciliation problem upon admission to ICU Medication reconciliation problem upon patient transfer from ICU
Monitoring need	Therapeutic drug monitoring required Other monitoring need
Identification of adverse effects	Identification of an adverse drug event Identification of an adverse drug reaction

Description of pharmaceutical interventions

Pharmaceutical intervention	Description
Change medication	Change from the currently administered medication to an alternative medication Change medication to follow protocol/guideline Change medication according to patient clinical status
Dose Adjustment	Increase in dose or decrease dosing interval Decrease in dose or increase dosage interval Increase or decrease in duration of treatment Prescribe correct dose or timing instructions Change in loading dose or maintenance dose
Change in formulation or administration route	Prescribe alternative formulation Continue same formulation, administer through a different route
Change in instructions for drug administration	Change in timing of administration Change in rate of administration Change in diluent type or diluent volume Other drug administration advice
Discontinue or pause medication	Discontinue medication without substitution Pause medication
Addition of a medication	Add new medication as required Restart medication as needed
Monitoring need	Need for therapeutic drug monitoring Need for other laboratory monitoring Need for other patient monitoring

Appendix 3
Data Collection Tool

C. Drug-related problem classification	
Drug-related problem category	Drug-related problem cause
1. Drug Selection <input type="checkbox"/>	Inappropriate medication according to guidelines/formulary No indication for drug Inappropriate combination of medications Inappropriate duplication of therapeutic group or active ingredient No or Incomplete drug treatment despite existing indication Too many drugs/active ingredients prescribed for indication Inappropriate medication based on the patient's clinical status
2. Drug Form <input type="checkbox"/>	Inappropriate drug form/formulation for this patient Another drug formulation/route of administration more appropriate for this patient
3. Dose selection <input type="checkbox"/>	Dose too low Dose of a single active ingredient too high Dosage regimen not frequent enough Dosage regimen too frequent Dose timing instructions wrong, unclear, or missing
4. Treatment duration <input type="checkbox"/>	Duration of treatment too short Duration of treatment too long
5. Dispensing <input type="checkbox"/>	Prescribed medication not available Wrong drug or strength made available at ward
6. Drug use process/drug administration <input type="checkbox"/>	Inappropriate timing of administration or dosing intervals by a healthcare professional Drug under-administered by a healthcare professional Drug over-administered by a healthcare professional Drug not administered at all by a healthcare professional Wrong drug administered by a healthcare professional Drug administered via the wrong route by a healthcare professional Inappropriate parenteral/enteral drug administration method
7. Patient-related <input type="checkbox"/>	Patient physically unable to use drug/form as directed
8. Patient-transfer related <input type="checkbox"/>	Medication reconciliation problem upon admission to ICU – medications that need to be continued/stopped upon admission Medication reconciliation problem upon patient transfer from ICU – medications that need to be continued/stopped/changed upon transfer
9. Monitoring <input type="checkbox"/>	Therapeutic drug monitoring required Other monitoring need
10. Identification of adverse effects <input type="checkbox"/>	Identification of an adverse drug event Identification of an adverse drug reaction
Source: Pharmaceutical Care Network Europe Association (PCNE). Classification for drug-related problems V9.1 [Online]. Basel: PCNE; 2020 [cited 2023 Jan 26]. Available from URL: https://www.pcne.org/upload/files/417_PCNE_classification_V9-1_final.pdf	

D. Pharmaceutical intervention classification	
Pharmaceutical intervention category	Pharmaceutical intervention description
Change medication <input type="checkbox"/>	Change from the currently administered medication to an alternative medication Change medication to follow protocol/guideline Change medication according to patient clinical status
Change in dose (dose adjustment) <input type="checkbox"/>	Increase in dose or decrease in dosing interval Decrease in dose or increase in dosing interval Increase or decrease in duration of treatment Prescribe correct dose or timing instructions Change in loading dose or maintenance dose
Change in formulation or administration route <input type="checkbox"/>	Prescribe alternative formulation Continue same formulation, administer through a different route
Change in instructions for drug administration <input type="checkbox"/>	Change in timing of administration Change in rate of administration Change in diluent type or diluent volume Other drug administration advice
Discontinue or pause medication <input type="checkbox"/>	Discontinue medication without substitution Pause medication
Addition of a medication <input type="checkbox"/>	Add new medication as required Restart medication as needed
Monitoring need <input type="checkbox"/>	Need for therapeutic drug monitoring Need for other laboratory monitoring Need for other monitoring

E. Categorisation of medications involved in DRP and PI corresponding to ATC code first level	
Alimentary tract and metabolism	<input type="checkbox"/>
Blood and blood-forming organs	<input type="checkbox"/>
Cardiovascular system	<input type="checkbox"/>
Dermatological	<input type="checkbox"/>
Genitourinary system and sex hormones	<input type="checkbox"/>
Systemic hormonal preparations	<input type="checkbox"/>
Anti-infectives for systemic use	<input type="checkbox"/>
Antineoplastic and immunomodulating agents	<input type="checkbox"/>
Musculoskeletal system	<input type="checkbox"/>
Central nervous system	<input type="checkbox"/>
Antiparasitic products	<input type="checkbox"/>
Respiratory system	<input type="checkbox"/>
Sensory organs	<input type="checkbox"/>
Various	<input type="checkbox"/>

F. Impact of pharmaceutical intervention on patient outcomes	
Prevention of a potential adverse drug event (pADE)	<input type="checkbox"/>
Achieving therapeutic serum concentration of medication	<input type="checkbox"/>
Fluid management	<input type="checkbox"/>
Improved efficacy / Therapeutic optimisation	<input type="checkbox"/>

G. Evaluation of pharmaceutical intervention in relation to prevention of a potential adverse drug event (pADE)		
pADE score using Nesbit method ¹ probability of an ADE occurring in the event the pharmaceutical intervention was not done		
Probability of ADE occurring (probability score)	Explanation of probability ^{2,3,4}	Examples ^{2,3,5,6,7}
High (0.6) <input type="checkbox"/>	<u>Harm is expected, life-threatening;</u> Ex: prevented a potentially fatal or severe reaction, ex: 10 times normal dose; narrow therapeutic range, life-threatening reaction/anaphylaxis	Ex. Overdose of low molecular weight heparin Ex. Omission of valaciclovir during ICU admission in a bone marrow transplant patient Ex. Patient prescribed amiodarone while currently taking digoxin without reduction in digoxin dose Ex. Enoxaparin and rivaroxaban both prescribed as regular treatment
Medium (0.4) <input type="checkbox"/>	<u>Harm is expected, clinically relevant;</u> Ex: prevented a potentially serious reaction, allergy to drug ordered, no allergy information, no adjustment of renal failure	Ex. Continuation of metformin, ACE inhibitor, and spironolactone in a patient with acute renal failure
Low (0.1) <input type="checkbox"/>	<u>Some harm is expected, poorly clinically relevant;</u> Ex: prevented a potentially significant reaction, 2-4 times normal dose, dose inadequate to produce a therapeutic effect, incorrect schedule/route with potential for therapeutic failure/toxicity, duplicate therapy with potential for additive toxicity	Ex. the need for therapeutic drug monitoring of levetiracetam, indicated because of the impaired renal function Ex. Patient takes an antibiotic twice daily when the recommended dose would be three times daily
Very low (0.01) <input type="checkbox"/>	<u>Some harm is expected, but not clinically relevant;</u> ex. problem orders, clarifications, missing information, missing strengths etc.	Ex. intravenous administration of a proton pump inhibitor, whereas oral administration is possible for the patient
Zero (0) <input type="checkbox"/>	<u>Information only, no harm expected</u>	Ex. two types of parenteral nutrition prescribed but only one administered to the patient Ex. Pharmacist suggests changing patient from esomeprazole to omeprazole exclusively for economic reasons

pADE = potential adverse drug event

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³ Saokaew S, Maphanta S, Thangsomboon P. Impact of pharmacist's interventions on cost of drug therapy in intensive care unit. *Pharmacy Practice (Granada)*. 2009;7(2):81-87.

⁴ Dong PTX, Pham VTT, Dinh CT, Le AV, Tran HTH, Nguyen HTL, et al. Implementation and Evaluation of Clinical Pharmacy Services on Improving Quality of Prescribing in Geriatric Inpatients in Vietnam: An Example in a Low–Resources Setting. *Clinical Interventions in Aging*. 2022;17:1127-1138. doi: 10.2147/CIA.S368871

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⁶ Kearney A, Halleran C, Walsh E, Byrne D, Haugh J, Sahm LJ. Medication Reviews by a Clinical Pharmacist at an Irish University Teaching Hospital. *Pharmacy*. 2017;5(4):60.

⁷ Gallagher J, Byrne S, Woods N, Lynch D, Mccarthy S. Cost-outcome description of clinical pharmacist interventions in a university teaching hospital. *BMC Health Services Research*. 2014;14:177.

Appendix 4

Validation questions for the data collection tool

Validation of the data collection tool as part of the dissertation entitled ‘Quality Evaluation of Clinical Pharmacy Services in an Intensive Care Unit’ by Ruth Agius

Dear Colleague,

Thank you for accepting to participate in the validation of the data collection tool which is part of the research project entitled ‘Quality Evaluation of Clinical Pharmacy Services in an Intensive Care Unit’.

Your input will assist in validating and adapting the data collection tool for use in the Intensive Care Unit. The aim of this tool is to capture and classify drug-related problems, pharmaceutical interventions, and outcomes, and to help evaluate their possibility of preventing a potential adverse drug event.

Kindly indicate if you would modify, add or remove any sections in the Data Collection Tool for Evaluation of Pharmaceutical Interventions

1. Patient Demographics

Kindly indicate if you would modify or remove any sections, giving reasons in the details column. Please also indicate if there are other essential data you would add to this section, giving details in the final row of the table.

Data required	Modify or Remove	Details
Date		
Intervention number		

Patient Demographics		
Gender		
Age bracket		
Weight		
Height		
Creatinine Clearance		
Dialysis Mode		
Other pertinent lab results		
Other important data to be added to this section:		

2. Details of Drug-Related Problem and Pharmaceutical Intervention

Kindly indicate if you would modify or remove any sections, giving reasons in the details column. Please also indicate if there are other essential data you would add to this section, giving details in the final row of the table.

Data required	Modify or Remove	Details
Context		
Drug-related problem		
Pharmaceutical Intervention		
Other important data to be added to this section:		

3. Drug-related Problems Classification

Each Drug-related problem category involves one or more types of drug-related problems.

For each type of drug-related problem, kindly indicate if there are any sections you would modify or omit, giving reasons for omission or details of modification in the reasons column. Kindly indicate if there are other essential drug-related problems to be added to the specific category, giving details in the final row of the table

Category 1: Drug Selection

Type of Drug-related problem	Modify or Remove	Reasons
Inappropriate medication according to guidelines/formulary		
No indication for drug		
Inappropriate combination of medications		
Inappropriate duplication of therapeutic group or active ingredient		
No or incomplete drug treatment in spite of existing indication		
Too many drugs/active ingredients prescribed for indication		
Other drug-related problems to be added to this category:		

Category 2: Drug form

Type of Drug-related problem	Modify or Remove	Reasons
Inappropriate drug form/formulation for this patient		
Other drug-related problems to be added to this category:		

Category 3: Dose Selection

Type of Drug-related problem	Modify or Remove	Reasons
Dose too low		
Dose of a single active ingredient too high		
Dosage regimen not frequent enough		
Dosage regimen too frequent		
Dose timing instructions wrong, unclear or missing		
Other drug-related problems to be added to this category:		

Category 4: Treatment duration

Type of Drug-related problem	Modify or Remove	Reasons
Duration of treatment too long		
Duration of treatment too short		
Other drug-related problems to be added to this category:		

Category 5: Dispensing

Type of Drug-related problem	Modify or Remove	Reasons
Prescribed medication not available		
Necessary information not provided or incorrect advise		
Wrong drug or strength dispensed		
Other drug-related problems to be added to this category:		

Category 6: Drug use process/Drug administration

Type of Drug-related problem	Modify or Remove	Reasons
Inappropriate timing of administration or dosing intervals by a healthcare professional		
Drug under-administered by a healthcare professional		
Drug over-administered by a healthcare professional		
Drug not administered at all by a healthcare professional		
Wrong drug administered by a healthcare professional		
Drug administered via the wrong route by a healthcare professional		
Other drug-related problems to be added to this category:		

Category 7: Patient-related

Type of Drug-related problem	Modify or Remove	Reasons
Patient physically unable to use drug/form as prescribed		
Other drug-related problems to be added to this category:		

Category 8: Patient Transfer Related

Type of Drug-related problem	Modify or Remove	Reasons
Medicine reconciliation problem upon admission to ICU		
Medicine reconciliation problem upon patient transfer from ICU		
Other drug-related problems to be added to this category:		

Category 9: Monitoring

Type of Drug-related problem	Modify or Remove	Reasons
Therapeutic drug monitoring required		
Other inappropriate outcome monitoring		
Other monitoring need		
Other drug-related problems to be added to this category:		

Kindly indicate if there are any major drug-related problems categories you would add or remove from the data collection tool

Other categories of drug-related problems to add

Categories of drug-related problems to remove

4. Pharmaceutical Intervention Classification

Each pharmaceutical intervention category involves one or more types of interventions.

For each type of pharmaceutical intervention, kindly indicate if there are any sections you would modify or omit, giving reasons for omission or details of modification in the reasons column. Kindly indicate if there are other essential pharmaceutical interventions to be added to the specific category, giving details in the final row of the table.

Kindly also check that pharmaceutical interventions can correlate with drug-related problems.

Category: Change in medication

Type of pharmaceutical intervention	Modify or Remove	Reasons
Change from the currently administered medication to an alternative medication		
Change medication to follow protocol/guideline		
Change medication according to patient clinical status		
Other pharmaceutical interventions to be added to this category:		

Category: Change in dose (Dose adjustment)

Type of pharmaceutical intervention	Modify or Remove	Reasons
Increase in dose or decrease in dosage regimen		
Decrease in dose or increase in dosage regimen		
Increase or decrease in duration of treatment		
Change in loading dose or maintenance dose		
Other pharmaceutical interventions to be added to this category:		

Category: Change in formulation or administration route

Type of pharmaceutical intervention	Modify or Remove	Reasons
Prescribe alternative formulation		
Continue same formulation, administer through a different route		
Other pharmaceutical interventions to be added to this category:		

Category: Change in instructions for drug administration

Type of pharmaceutical intervention	Modify or Remove	Reasons
Change in timing of administration		
Change in rate of administration		
Change in diluent type or diluent volume		
Other change in drug administration advice		
Other pharmaceutical interventions to be added to this category:		

Category: Discontinue or pause medication

Type of pharmaceutical intervention	Modify or Remove	Reasons
Discontinue medication without substitution		
Pause medication		
Other pharmaceutical interventions to be added to this category:		

Category: Addition of a new medication

Type of pharmaceutical intervention	Modify or Remove	Reasons
Add new medication as required		
Restart medication as needed		
Other pharmaceutical interventions to be added to this category:		

Category: Monitoring need

Type of pharmaceutical intervention	Modify or Remove	Reasons
Need for therapeutic drug monitoring		
Need for other laboratory monitoring		
Other pharmaceutical interventions to be added to this category:		

Other categories of pharmaceutical interventions to add

Categories of pharmaceutical interventions to remove

5. Outcome of pharmaceutical intervention

Kindly indicate if categories are clear and if you would modify any categories

Category	Modify to
Prevention of a potential adverse drug event	
Achieving therapeutic serum concentration of medication	
Fluid management	
Improved efficacy / Therapeutic optimisation	

6. Evaluation of pharmaceutical intervention in relation to prevention of a potential adverse drug event (pADE)

Kindly indicate if you would amend the description of the Value of pADE by adding, modifying or removing any details.

Value of pADE	Description
High (0.6)	Harm is expected, life-threatening, prevented a potentially fatal or severe reaction, e.g. 10 times normal dose; narrow therapeutic range, life-threatening reaction/anaphylaxis
	Examples from literature: Overdose of low molecular weight heparin; omission of valaciclovir during ICU admission in a bone marrow transplant patient
Modify:	
Medium (0.4)	Harm is expected, clinically relevant, prevented a potentially serious reaction, e.g. allergy to drug ordered, allergy information, adjustment of renal failure
	Example from literature: Continuation of metformin and ACE inhibitor in a patient with acute renal failure
Modify:	
Low (0.1)	Some harm is expected, but poorly clinically relevant; e.g. prevented a potentially significant reaction, 2-4 times normal dose, dose inadequate to produce a therapeutic effect, incorrect schedule/route with potential for therapeutic failure/toxicity, duplicate therapy with the potential for additive toxicity
	Example from literature: the need for therapeutic drug monitoring of levetiracetam, indicated because of impaired renal function

Modify:	
Very low (0.01)	Problem orders, clarifications, missing information etc.
	Example from literature: intravenous administration of a proton-pump inhibitor whereas oral administration is possible
Modify:	
Zero (0)	Information only, no harm expected
	Example from literature: two types of parenteral nutrition prescribed but only one administered
Modify:	

Kindly indicate if addition of examples for each section could facilitate the evaluation of the probability of pADE (examples from published studies)

7. Classification of medications involved according to ATC Classification First Level, kindly indicate if you would modify the classification

Classification of medications involved in drug-related problems according to ATC code level 1
Modify:

Finally, kindly indicate if there are any other categories or sections you would add, modify or remove to the data collection sheet to be able to capture drug-related problems, pharmaceutical interventions and evaluation of interventions in the intensive care unit.

Add
Modify
Remove

Do you have any further suggestions?

Appendix 5
Dissemination of findings

Abstract presented as a poster presentation at the 28th Congress of the European Association of Hospital Pharmacists in March 2024

Development and validation of a data collection tool to evaluate pharmaceutical interventions in an intensive care unit

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Background and importance

Clinical pharmacy services have been recently introduced in intensive care unit (ICU) and consequently, service evaluation is anticipated. There is the need for a tool to capture pharmaceutical interventions in ICU and assess their impact on specific patient outcomes.

Aim and objectives

To develop and validate a tool to describe and classify drug-related problems (DRPs) and Pharmaceutical Interventions (PIs) in ICU and evaluate the probability of the PI in preventing a potential Adverse Drug Event (pADE).

Materials and methods

A classification system based on Pharmaceutical Care Network Europe (PCNE) V9.1 was identified to capture and resolve DRPs identified in ICU. The PCNE V9.1 classification provides extensive categories of DRPs. Evaluation of impact of PIs in preventing a pADE is conducted using an established score¹. The pADE score reflects the likelihood of an ADE occurring in the absence of a PI. The developed data collection tool was validated by an expert panel made up of three clinical pharmacists practising in ICU and a consultant intensivist. The expert panel assessed the tool for face and content validity and practicality in ICU setting. Subsequently, the tool was piloted in ICU for ten days.

Results

The data collection tool consists of seven sections namely patient demographics with details about pertinent laboratory results, description of DRP and PI, classification of DRP and PI, outcome of PI, and categorisation of medications involved. The final section of the tool relates to evaluation of PI in relation to prevention of a pADE and contains five categories, zero to high, which correspond to the probability of a pADE occurring if the pharmacist had not intervened. Examples from literature are presented for each pADE category to assist with the evaluation of PIs. Following validation and pilot testing, four sections were amended to better adapt the tool to ICU setting.

Conclusion and relevance

The development of such a data collection tool is important to standardise the classification of DRPs and interventions recommended by pharmacists in ICU. The tool contributes to data demonstrating value of pharmacist interventions on patient outcomes.

References

1. Nesbit TW, et al. Implementation and pharmacoeconomic analysis of a clinical staff pharmacist practice model. *AJHP* 2001;58(9):784–790.

Citation

Agius R, Vella Szijj J, Azzopardi L. 4CPS-203 Development and validation of a data collection tool to evaluate pharmaceutical interventions in an intensive care unit. *European Journal of Hospital Pharmacy* 2024;31:A149-A150. doi: <https://doi.org/10.1136/ejhpharm-2024-eahp.307>

Evaluation of pharmaceutical interventions in an intensive care unit

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Introduction

Due to complex pharmacotherapy often involving high-risk medications and the severity of the illness, critically ill patients are more vulnerable to adverse drug events. Pharmacists' participation in Intensive Care Units (ICUs) has shown to improve patients' clinical outcomes when being directly involved in patient care, as members of the multidisciplinary team. The aim of this study was to evaluate the activities of clinical pharmacists in a mixed intensive care unit of an acute general hospital by assessing pharmaceutical interventions and their impact on surrogate clinical outcomes.

Method

A data collection tool was developed and validated to capture and classify drug-related problems (DRPs) and pharmaceutical interventions (PIs) suggested by pharmacists in ICU where a clinical pharmacy service has been operating for two years. Data on DRPs and PIs recommended by a team of pharmacists over 3 months in the ICU, was collected and recorded in the data collection tool. A sample of DRPs and PIs were categorised and evaluated by an expert panel of healthcare professionals to assess the probability of a potential adverse drug event (ADE) occurring in the absence of the PI.

Results

The ICU pharmacist-patient profiles of 164 patients were included in this study, where 484 DRPs were identified in 135 patients; 38% were related to dose selection, 24% involved drug selection, and 13% were related to need for monitoring. Most suggested PIs were related to adjustment in medication doses (40%), addition of medication (17%), and monitoring (16%). Anti-infectives for

systemic use were the most common group of medications identified in DRPs (41%). PIs were categorised according to their impact on surrogate patient outcomes. Pharmacists assisted in optimising fluid management for 17 patients, which involved hidden fluids in parenteral infusions, IV to PO conversions, and adjusting enteral feed. Therapeutic drug monitoring was recommended for 43 patients with subsequent dose adjustment to achieve therapeutic serum concentrations for medications with a narrow therapeutic range, including aminoglycosides, vancomycin, antiepileptic medications, and digoxin.

From the 113 PIs evaluated by the expert panel, 31 were found to have a medium probability and 63 were assessed as having a low probability in preventing a potential ADE. The remaining 19 PIs had very low or zero probability of preventing a potential ADE. Interventions evaluated to have a medium probability of preventing a potential ADE included adjustment of medication doses and dosing intervals for nephrotoxic antibiotics, thus, preventing further risk of nephrotoxicity, and suggesting ECG monitoring and subsequent medication change due to drug-drug interactions causing prolonged QTc interval, thus potentially preventing arrhythmias.

Conclusion

The study has indicated that pharmacists' interventions in the ICU are effective in reducing the risk of occurrence of potential ADEs. Whilst the risk impact was estimated to be ranging between medium to very low, a key aspect in patient-centric care is providing optimised pharmacotherapy to mitigate individual patient risks as a result of medication use. The study has demonstrated the outcome of activities within the multidisciplinary team in the ICU on surrogate clinical outcomes.