Risk Minimisation Strategies Through Drug Utilisation Review

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To my family

Mariano Jr., Blandina, Romar, and Jeff

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Abstract

The Pharmacy-Of-Your-Choice (POYC) scheme is a national pharmaceutical service that provides free medicines and medical devices to outpatients in Malta through 219 private community pharmacies. The POYC unit prioritises completing pharmacy administrative requirements when approving entitlement to medicines. According to the POYC database, over 14,000 senior adults were prescribed 10 or more drugs to treat a variety of conditions. Clinical services are required for several therapies to provide care continuity across the healthcare system. This study aimed to evaluate and characterise the process of pharmacists' clinical review at the POYC entitlement unit and to develop a risk minimization strategy through a drug utilisation review. A focus group discussion was organised to understand needs, advantages, barriers, experiences, and prioritisation of a clinical review process within the POYC entitlement unit. Using the information gathered, a Drug Utilisation Review tool feasible for the POYC setting was developed. The tool was validated and applied to a retrospective drug utilisation review of 150 patients (60% male, 40% female) receiving at least 10 entitled medications. The risk of identified drug-related problems for 10 patient cases was assessed by a panel composed of pharmacists and medical practitioners through a matrix table with the "probability" and "consequence" risk ratings on a scale of 1 to 5, indicating very low, low, moderate, high, and very high risk respectively. "Consequence" is the potential outcome of the drug-related problem, while "probability" is an estimate of the chance of an event or an incident happening. Very low-risk drug-related problems require no treatment. Low risk requires self-care, moderate risk is DRPs requiring medical treatment, high risk may require hospital treatment and very high-risk DRPs cause death

and permanent disability. From the focus group discussion, patients with multiple conditions and managed with multiple consultants, and with at least 10 medications were identified for prioritisation in the DUR process. From the patient DURs carried out, 84% (n=126) had 10–15 entitled medications with aspirin (67%), amlodipine (61%), omeprazole (58%), metformin (55%), bumetanide (52%), and perindopril (47%) as the most frequently prescribed medications. Hypertension (81%), diabetes mellitus type 2 (58%), and ischaemic heart disease (53%) were the top medical conditions. The main drug-related problems requiring intervention at the prescriber and patient levels identified by the DUR process were potential drug interaction (34%), risk of adverse drug reactions (21%), and potentially unnecessary drug therapy (20%). The most common median risk scores for drug-related problems were 3, 4, and 5, indicating a moderate, high, and very high medication risk, respectively. When used in conjunction with the patient prioritising criteria, the DUR tool results in a systematic pharmacist intervention towards a clinical role during the POYC entitlement appraisal procedure.

Keywords: medication risk, drug related problems, clinical pharmacy

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List of Abbreviations

ADR	Adverse Drug Reactions
CRM	Comprehensive Medication Review
CVD	Cardiovascular Disease
DRP	Drug Related Problem
DUR	Drug Utilisation Review
FGD	Focus Group Discussion
GFL	Government Formulary List
IMPACT	Improving Medicines and Polypharmacy Appropriate Clinical Tool
IQR	Interquartile Range
MAS	Medicine Approval Section
MUR	Medication Use Review
NICE	National Institute for Health and Care Excellence
POYC	Pharmacy Of Your Choice
POYC-MAS	Pharmacy Of Your Choice – Medicine Approval Section
START	Screening Tool to Alert to Right Treatment
STOPP	Screening Tool of Older Persons' Prescriptions
WHO	World Health Organization

Chapter 1

Introduction

1.1 Setting the scene: Pharmacy Of Your Choice (POYC)

The Pharmacy of Your Choice (POYC) is a nationwide pharmaceutical service provider in Malta, providing free government-supplied medicines and pharmaceutical equipment to approximately 140,000 outpatients through 219 community pharmacies. [1] A person suffering from one of the diseases or conditions specified in Part II of the Fifth Schedule of Social Security Act (Chapter 318) Article 23 and its amendment - Act No. I of 2012[2], "shall be entitled to such Free Medical Aid according to protocols which may be issued by the Chief Government Medical Officer from time to time and are available within the national health service". For patients to access the medicines for free, they need to get approval of entitlement for each medication. The Pharmacy of Your Choice – Medicines Approval Section (POYC-MAS) reviews and approves applications from prescribers for outpatients premised on the Government Formulary List (GFL) to ensure conformance and making sure that the entitlement is applied across the board. Applications for free medicines are determined based on indications, prescriber parameters, circumstances that classify individuals for therapy, diagnostics indicated prior to treatment, measurable indicators of effectiveness, and any additional disclosures that may be required. [3]

[1] Government of Malta. Pharmacy of Your Choice About Us [Internet]. Malta: Ministry of Health; 2020 [cited 2021 Dec 23]. Available from URL:https://deputyprimeminister.gov.mt/en/poyc/Pages/About%20Us.aspx

[2] Government of Malta. Chapter 318: Social Security Act [Internet]. Malta; 1987 [cited 2022 Jan 10]. Available from URL: https://deputyprimeminister.gov.mt/en/pharmaceutical/Documents/cap_318.pdf

[3] Government of Malta. Pharmacy of Your Choice Medicines Approval[Internet]. Malta: Ministry of Health; 2020 [cited 2021 Dec 28]. Available from URL: https://deputyprimeminister.gov.mt/en/poyc/Pages/360%C2%B0-One-Stop-Shop-Service-Concept/Medicines-Approval/Introduction.aspx

The approval of medicines for chronic use within the national health service scheme relies on patients receiving medicines from a formulary according to condition protocols prioritizing pharmacy administrative processes. Upon completion of the administrative process, patients will receive the necessary notification from the POYC unit in the form of a yellow card listing the medicines/pharmaceuticals to be collected from their chosen pharmacy every 56 days.[4] Figure 1.1 summarises the pharmacy administrative process for free medicine entitlement approval in the POYC scheme.

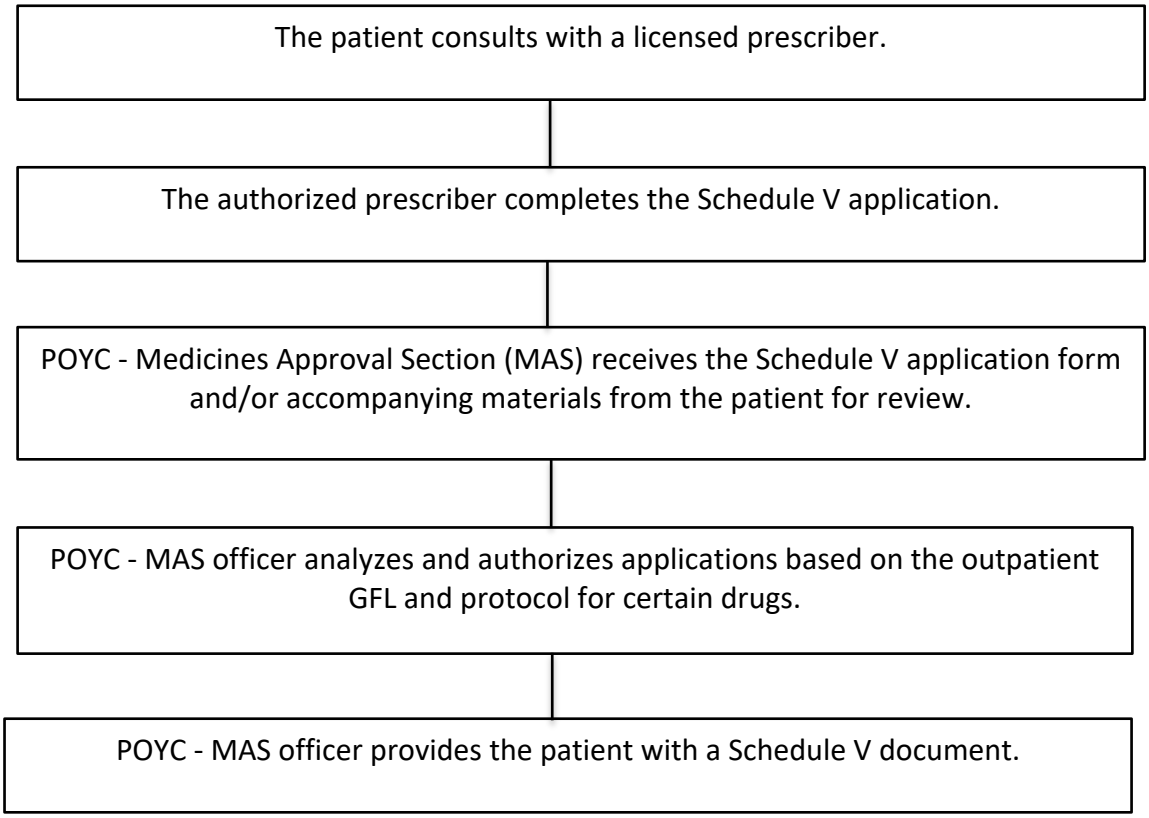

Figure 1.1 Schematic diagram of entitlement application

[4] Government of Malta. Pharmacy of Your Choice FAQs[Internet]. Malta: Ministry of Health; 2020 [cited 22 Jan 10]. Available from URL: https://deputyprimeminister.gov.mt/en/poyc/Pages/POYC-Scheme/Frequently-Asked-Questions.aspx

1.2 Medication risks

Patients who receive free medication through the POYC scheme, particularly the elderly, are prone to polypharmacy. Polypharmacy is the patient's utilization of numerous medications to treat various conditions that potentially result in drug-related issues. From the database of the Survey of Health, Ageing, and Retirement in Europe (SHARE), participants with the age of 65 years or more take 5 or more medications per day resulting to the prevalence of polypharmacy of 26.3% as the lowest and 39.9% as the highest across Europe (Midão et al, 2018).

Determinants of polypharmacy as shown in previous research include increased body mass index (Bardel et al, 2000), obesity and the cardiovascular comorbidities (Davin et al, 2012; Guillot et al, 2015), elderly population with lower educational level (Plaza-Zamora et al, 2020), female gender (Ayalew, 2019), place of residence, ethnicity, behavior (Guillot et al, 2015). A meta-analysis that includes forty-seven studies showed that six to nine medications and excessive polypharmacy were significantly associated with death as a consequence (Leelakanok, 2017). The rise of medications prescribed to patients consistently resulted in an increased rate of hospitalization and mortality across subgroups of age, residential area, and comorbidities when compared to patients taking one or two medications (Chang et al, 2020).

Polypharmacy and certain drug classes like thiazides, antidepressants, benzodiazepines, and anticonvulsants are associated with the frequency of drug-related problems (DRPs)

among older adults presenting to the emergency department with non-specific complaints (Nickel et al, 2013). A study by Mejía et al (2020) showed that 8.4% of urgent hospital admissions were attributed to an ADR, making age, comorbidities, and polymedication the main risk factors. In another study done by Pérez Menéndez-Conde et al (2011), ADR caused 19.4 percent of admissions and 65 percent of them might have been avoided. Nivya et al (2015) found that antineoplastic therapy and immunosuppressants were responsible for 38% of ADR, with 20.4% of hospitalizations requiring transfer to the intensive care unit (ICU) or resulting in irreversible harm. Ayalew (2019) mentioned that antithrombotic medications, antihypertensive pharmaceuticals, analgesics, anti-diabetics, antipsychotics, and anti-neoplastic drugs produce 1.3% to 41.3% of drug-related. One-third of drug-related hospital admissions might have been prevented, and more than 40% could have been avoided .

From the study of Linkens et al (2020), multiple risk factors for medication-related admissions and readmissions are observed in studies, including polypharmacy, comorbidities, therapy lack of adherence, memory deficits, living circumstances, high-risk drugs, and greater age. Even with preventable drug-related problems, when not detected early enough, they can lead to hospitalization. The possibility of admission as a consequence of DRP, particularly in elderly patients on polypharmacy, may be avoided when risk reduction procedures to avoid a spike in treatment cost and prevent complications are given a high priority.

1.3 Necessity to promote clinical pharmacy service

The POYC's administrative services, which currently distribute pharmaceuticals to a large number of patients, should be expanded to include patient-centered tasks. Patients receiving multi-morbid condition treatment for long-term use may benefit from a clinical review that promotes improving drug safety, particularly for senior patients. POYC's long-term use prescriptions delivered through community pharmacies should be re-evaluated for drug adherence and therapeutic appropriateness, particularly when a new treatment is added. In earlier years, small-scale study was conducted in Malta, with consistent results demonstrating the necessity of taking the time to monitor medication used by patients over time. Through the POYC scheme, Vella et al (2011) identified 39% of pharmaceutical side effects and 24% of patients who were at risk of clinically severe drug interactions from a specific community pharmacy. In southern Malta, Bugeja et al (2013) discovered 225 drug interactions at village community pharmacies. Mifsud et al (2019) identifies 481 drug-related problems through a pharmacist-led medication use review in community pharmacy for patients on warfarin were identified that require monitoring, compliance and patient education.

Medication-related research were also conducted in a hospital setting in Malta. Seychell and Weidmann (2018) found 498 prescription errors at Karin Grech Hospital, while Camilleri et al (2019) detected 194 drug-related issues in the Diabetic Hospital Out-Patient Clinic's ambulatory clinical pharmacist service. In a study done by Farrugia et al (2017), 12.3% of hospitalizations were attributable to drug induced adverse effects, with

the 70–89-year-olds being the most common age group affected. Antihypertensive medications, psychiatric pharmaceuticals, and diabetic drugs were responsible for 21, 15, and 9 drug-induced admissions, respectively. Overdose toxicity and side effects were found to be prevalent in all age categories, except in the 'younger than 49 age group,' where unintentional and suicide ingestion were the predominant classifications. In the risk assessment exercise, all four pharmacists and two physicians assigned a score of 15 or higher to at least one case, signaling the need for early intervention.

Based on the data gathered on the risks posed by prescribed treatments in both the community and hospital environment, this calls for reinforced clinical services. Up to date, there have been no drug utilisation reviews practised as a structured procedure in POYC and in community pharmacies participating in the POYC scheme. A recommendation from a study by Ayran (2021) conducted in POYC showed that putting administrative tasks at the focus of the entitlement process encourages optimisation by adding clinical services like drug utilisation review to optimize safety and efficacy while preventing the potential risk of medicines approved for chronic use. Magno (2021) identified that when the pharmaceutical operations in the POYC scheme were examined, community pharmacists and patients expressed a high level of interest in an expanded POYC clinical service in primary care such as new medication evaluation. A study done by Cassar (2020) on the efficiency and sustainability of the POYC system, which provides patient access to drugs, found that unused medication cost €3,660 over 56 days, with financial and environmental ramifications. When a list of interventions was presented to pharmacists and patients to tackle the issues, the medicine review was

the most popular option among both pharmacists and patients (59.0%). With the 2022 agreement between the Ministry of Health and community pharmacies, community pharmacist-led medication reviews are going to be undertaken and the financial implications are covered by the government.

The goal of clinical review in POYC is to lower the economic burden on the healthcare system while integrating patient-centered approaches where potential drug-related problems can be identified and corrected before medicine reaches the patient.

1.4 Risk Minimisation Strategies

Patients taking long-term medicines need to have their regimens evaluated and renewed. The removal of superfluous medication or the inclusion of another drug are two common changes that might be performed (Vella & Azzopardi, 2011). Patients may require medication review during maintenance therapy, particularly if they are receiving treatment from many healthcare providers (Blenkinsopp et al, 2012). It is especially important to note that some people may not take their medications as prescribed or may have difficulty controlling their own medications.

Different interventions are being researched by Linkens et al (2020) to cut down on the number of medication-related readmission rates. A few of these intervention strategies, such as pharmacist engagement, education programs, and transition-of-care

interventions, as well as the use of digital assistance in the form of Clinical Decision Support Systems, may lessen readmissions.

A key risk-minimization method is to identify risk factors for drug-related complications. For instance, the quantity of medications used, comorbidities, use of high-risk medications, special populations, and polypharmacy are all risk factors. The risk factors obtained could support pharmacists to systematically characterise and detect patients at risk for DRPs, as well as direct and focus on preventative interventions to restrict the occurrence of DRPs. According to Kaufmann et al (2015), established risk factors could also serve as the foundation for a screening tool to identify patients at risk for DRPs. Other strategies studied by Lavan and Gallagher (2016) include executing an organised medication review with the goal of optimising pharmacotherapy, or using efficient software engines that can reliably and quickly undertake complex drug reviews in elderly multimorbid and fragile patient populations.

Various drug-utilization or medication review tools are available to identify different drug-related problems tailored to the applicability to the setting of review, population, age, gender, and conditions. The STOPP/START criterion, which structures physiological systems such as the cardiovascular and central nervous systems to examine possibly inappropriate drugs in older people, is one of the most extensively utilised criteria (Sallevelt et al, 2020; O'Connor, 2021). The Amsterdam tool is another systematic, thorough, and practical tool that comprises a full checklist of numerous drug-related difficulties divided into physiological systems and illnesses, as well as a structured script

for guided patient interviews (Mast et al, 2015). "Polypharmacy Guidance, Realistic Prescribing" is one of the clear guidelines that provide direction on limiting incorrect polypharmacy while starting new treatments or reviewing existing ones. [5] "Improving Medicines and Polypharmacy Appropriateness Clinical Tool (IMPACT)" provides practical guidance on how to appropriately stop, discontinue, withdraw a medicine and factors to consider to avoid medication-related harm. [6]

Another method of reducing medication risk is through medication reconciliation. It is the process of identifying and preventing inadvertent discrepancies and patient damage between patients' medication lists as they move through different stages of care (Kwan et al, 2013; Mekonnen et al, 2016). In comparison to standard care, medication review in conjunction with medication reconciliation, patient education, professional education, and transitional care was linked to a lower incidence of rehospitalization (Dautzenberg et al, 2021).

1.5 Impact of Drug Utilization Review

The central goal of a medication review is to reduce medication-related preventable harm, reduce financial burden, and improve patient quality of life despite chronic illness

[5] Scottish Government Polypharmacy Model of Care Group. Polypharmacy Guidance, Realistic Prescribing 3rd Edition [Internet]. Scottish Government. 2018. [cited 2022 Jan 15]. Available from URL: https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2018/04/Polypharmacy-Guidance-2018.pdf

[6] National Health Servise (NHS) PrescQIPP. IMPACT - Improving Medicines and Polypharmacy Appropriateness Clinical Tool [Internet]. United Kingdom: NHS; 2020. [cited 2022 May 19]. Available from URL:http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Clinical_Guidelines/clinical_guidelines_front_page/PrescQipp_IMPACT.pdf

(Blenkinsopp et al, 2012). Any healthcare provider is expected to contribute to the safety of the patient. As pharmaceutical experts, pharmacists, on the other hand, have the authority to shift from product- or business-centered practices to patient-centered practices. Pharmacists in a variety of healthcare settings play an important role in performing medication reviews to ensure medication safety, identify medication hazards, and plan a pharmacist intervention. Varas-Doval (2020) indicates that interventions from clinical pharmacists to solve DRP in an open-label multi-centered cluster randomized study in Spain largely involve the addition and change of a medicine, as well as educational interventions on medicine adherence and non-pharmacological measures.

Drug utilisation reviews will benefit not only polypharmacy patients, but also patients taking fewer high-risk medications. In the study of Shetty et al (2018), pharmacist-led drug utilisation review in patients with a minimum of two prescription medicines was reviewed, and the outcome showed that an increased number of medications was independently associated with the occurrence of drug interactions and not with the increased number of comorbidities. Providing a medication review with follow-up in collaboration with general practitioners and patients improves the health of elderly polypharmacy patients and shrinks challenges associated with medication use (Varas-Doval, 2020).

A clinical service's influence exists in specialized settings like clinics and nursing homes. In the study of Yates et al (2020), pharmacists' clinical intervention in a heart failure

clinic resulted in a significant decrease of DRPs from 2.80 to 1.95, indicating improved drug adherence and renal dosage. The maximum acceptance rates were for medication adherence (78%), renal dosage (67%), hypertension (58%), and HF DRPs (55%). As shown in a retrospective analysis of 422 nursing home residents in North East England, 298 (70.6 %) had at least one drug withdrawn, accounting for 704 tablets, or 19.5 percent of the 3602 originally prescribed (Baqir et al, 2017).

Despite the rise in client traffic at community pharmacies to accommodate both over-the-counter and prescription-only transactions, a clinical service remains attainable. Treatment compliance has been demonstrated to improve with the implementation of community pharmacist-led strategies, leading to better blood pressure, cholesterol, COPD, and asthma control (Milosavljevic et al, 2018). In a systematic review, medication reviews done by community pharmacists dramatically reduced the incidence of emergency department visits and hospitalizations when contrasted to routine care (Tasai et al, 2021).

Pharmacists collaborate with other professionals to contribute significantly with their clinical work. The physician's response determines how clinical findings are implemented to have an impact after a thorough medication review. The study of Basheti et al (2016) showed that in Jordan, physician-approved pharmacist's interventions for patients with chronic conditions caused a reduction in treatment non-adherence. In China, 91% of pharmacist-proposed interventions were adopted,

addressing 91.6 percent of drug-related issues found among hospitalized COPD patients (Li et al, 2019).

The hospital stay for admitted patients is another favourable effect of the drug use evaluation. In a Canadian trial, 6,416 high-risk patients received early pharmacist-led medication review and 4,391 underwent conventional care. The mean number of hospital days reflects an 8% reduction in the median duration of stay, with an additional 11% drop in patients under the age of 80 (Hohl et al, 2017).

Current insights on the impact of pharmacists in healthcare expenditure gained attention in research. The amount of money spent on treatments and preventing drug-related issues is growing, resulting in prescription errors and inappropriate prescribing as a healthcare strain. Because pharmacists have the competence to detect, address, and prevent prescription errors and pharmaceutical-related problems, this circumstance presents a big opportunity for their enhanced functions to have a significant impact on decreasing healthcare expenditures (Dalton and Byrne, 2017). This study illustrates that pharmacists can help save money on healthcare in a range of situations. In the study of Chen et al (2020), following pharmacist placement in the hematology unit, the average duration of hospitalization decreased from 19.27 days to 16.69 days, while the computed economic benefits, cost avoidance, and benefit-cost ratio grew. The pharmacist-led plan saved a peak value of US$20.49 over 6 months for very seriously injure with COPD in India, equating to a 30.6% reduction in medicine costs which was reduced to 26.1% when pharmacists' time (US$3.00/patient) was factored

(Abdulsalim et al, 2020). Pharmacist presence in the care of patients who arrive to the urgent care saves money on healthcare, especially in the areas of hands-on care and preventing adverse medication events. For critical care pharmacists, the possible financial benefit-to-cost ratio is between $1.4:1 to $10.6:1 (Rech et al, 2021). In the study of Jokanovic et al (2017) , significant decreases in medication and healthcare expenses were observed, implying good effects on glycosylated hemoglobin, blood pressure, cholesterol, and the amount and appropriateness of drugs.

Drug utilisation reviews, in general, have a positive impact on the healthcare system (Abrahamsen et al, 2020). Such a practice is appropriate in clinics, elderly homes, community pharmacies, and hospitals. POYC, as a sector that contributes to Malta's excellent health, is a promising platform to offer drug utilisation review as a clinical service.

1.6 Barriers in initiating drug utilisation review

Drug-utilization review is a clinical service put forward with the aim of improving treatment safety and efficacy. Barriers are key identifiers for not establishing the service. Acceptance of drug utilization review is still a challenge in some healthcare settings. Mc Namara et al (2017) argued that some healthcare practitioners were either unaware of or dismissed medical decision aids and measuring instruments that could help with these processes. Even while it contributes to patient safety, a few clinicians still express uneasiness when utilizing the DUR system in outpatient clinical settings

(Choi et al, 2014). A pharmacist-led medication review might be hindered by a lack of patients' confidence in pharmacists' expertise (Uhl et al, 2018).

Some healthcare workers avoided taking responsibility for multimorbidity management due to difficulties with coordinating, communication, and continuity of care, workload demands, and ambiguous individual duties for care. Enhanced care is advantageous in DUR service because of better culture, deployment of electronic health records, facilities, information systems, coordination of care and access, greater involvement of pharmacists, nurses, and patients, families in care delivery, and the use of care coordinators (Mc Namara et al, 2017; Stephenson et al, 2017). Workload, clear leadership, decision-making, limited institutional, organizational resources, the complex nature of the healthcare system, engagement, functionality of integrated care and collaboration, and positive impact, and clinical benefits, are among the additional domains outlined by healthcare professionals as relevant roadblocks to their experiences (Stephenson et al, 2017; Salas et al, 2020).

In a comprehensive medication review (CMRs) and post-discharge follow-up in elderly hospitalised patients conducted by Kempen et al (2020), the facilitators and barriers for doing CMRs were identified. The necessity of CMR for many, if not most, patients and the positive outcome of the service were the facilitators. Barriers include the scarcity of resources; pharmacists' lack of clinical experience; compatibility of CMRs with hospital practice; uncertain tasks and functions; and the need for personal contact in the care facility for physician-pharmacist collaboration.

When it comes to the variables that help or impede the growth of a medicine usage review service in Eastern Europe and Iran, the primary bottlenecks highlighted are the unfamiliarity with the service, a lack of money, and private consultation locations. Pharmacists in the Eastern-European countries and Iran are well-positioned to perform medication use reviews (MURs), but the service requires more promotion and hurdles, primarily at the organizational and regulatory levels, must be overcome (Tuula et al., 2021).

1.7 Rationale of the study

Clinical services such as medication review have emerged as an important complement to POYC services, according to preliminary studies. Magno (2021) advocated evaluating options for clinical services such as drug utilization review when reviewing POYC program services. The findings suggest that community pharmacists and patients have a high level of agreement on their receptivity to the idea of future clinical services such as medication review, and that this requires support from the POYC unit and medical practitioners. Ayran (2021) recommended optimizing the medicine approval system process by incorporating POYC pharmacists in drug use evaluation and medication therapy management in his study "The Review of POYC Medicines Approval System."

The POYC-MAS undertaking in approving protocol-based applications of medicine entitlement is limited to reviewing the specific criteria. The POYC-MAS platform is a one-of-a-kind platform for evaluating new treatment applications for drug-related issues

before they reach the patient. This is an opportunity for interprofessional collaboration and to take steps to ensure patient safety. With the addition of drug utilization as a clinical service to the administrative tasks, the POYC has an open opportunity to upgrade the healthcare system. Leading changes are dependent on the POYC's basic policies and culture, which necessitates the active participation of legislators and health care professionals, including pharmacists.

1.8 Aims and Objectives

This research aimed to evaluate the opportunities of pharmacists' clinical review at the Schedule V POYC entitlement unit and to develop a risk-minimization strategy through a drug-utilization review that ensures safe, rational use of medicines while optimizing patient access to therapy. The objectives of the study were to:

- Characterise pharmacists' review procedure at the POYC-MAS for optimising and lowering the likelihood of DRPs.
- Develop and validate a risk minimisation tool that can be utilised by pharmacists during drug entitlement review.
- Evaluate drug-related problems through drug-utilization review retrospectively.
- Assess the risk of identified drug-related problems.

Chapter 2

Methodology

2.1 Research overview

To attain the objectives of the study, the research was divided into three phases. The major steps of the research are summarized in Figure 2.1.

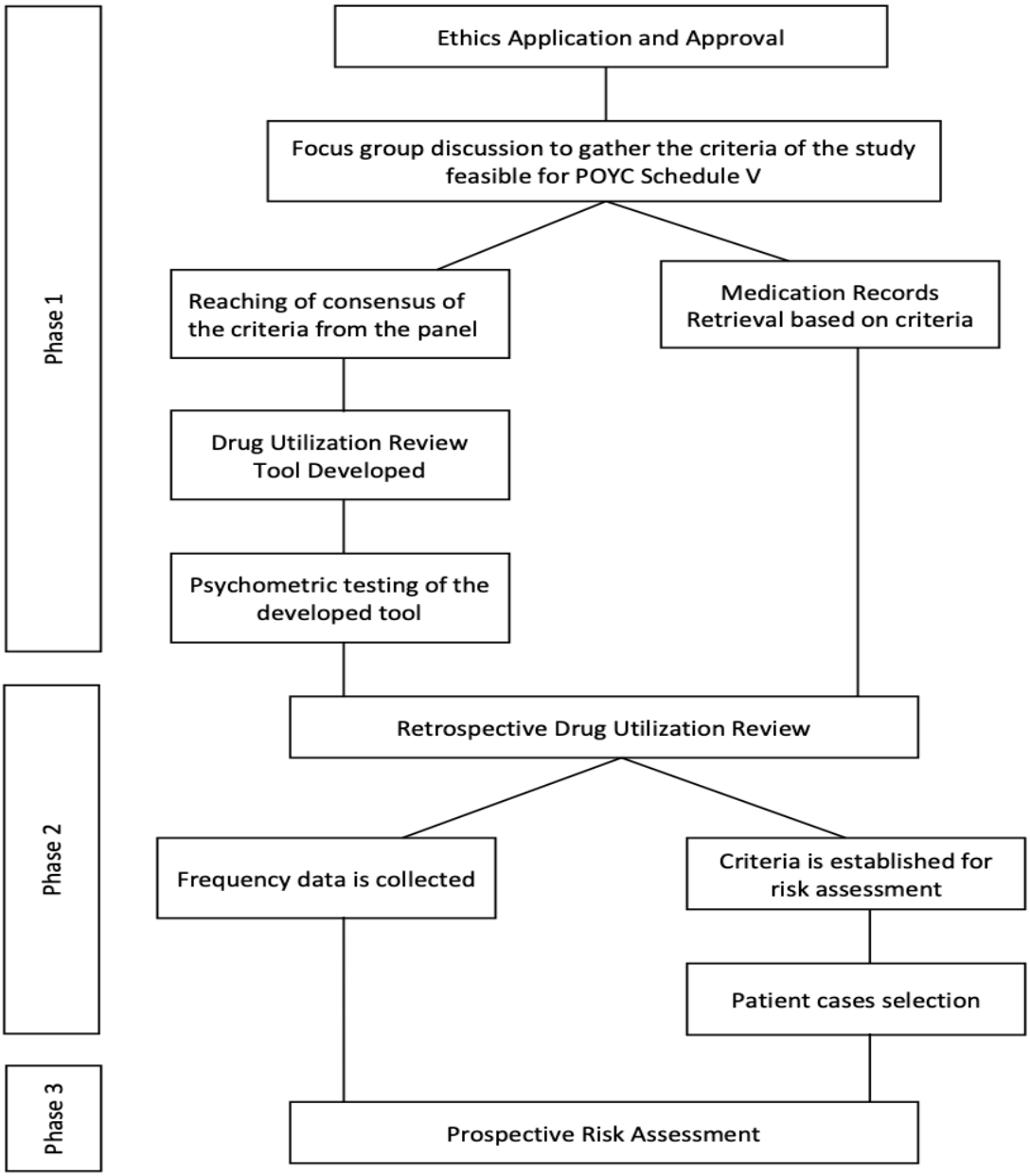

Figure 2.1 Schematic diagram of the key steps in the research

2.2 Research setting and design

The research was carried out at POYC, a national service provider in Malta that supplies free medications and pharmaceutical equipment to outpatients. The study employed a mixed approach with three stages, as shown in Table 2.1. Focus group discussions provided qualitative data, while the retrospective drug utilization review and prospective risk assessment provided quantitative data.

Table 2.1 Methodology Design

Phase	Research Objectives	Type of Data	Data Collection
1	To identify drug utilisation review prioritisation for pharmacist to optimise therapy and reduce risk of DRPs.	Qualitative	Focus Group Discussion
2	To use the developed drug-utilization review tool in identifying drug-related problems	Quantitative	Evidenced based medication review
3	To assess the risk of drug-related problems	Quantitative	Risk Matrix

2.3 Ethics application and approval

Necessary approvals were obtained from POYC. Ethics Approval was granted by the Faculty of Medicine and Surgery Research Ethics Committee (Appendix 1).

2.4 Phase 1: Focus Group Discussion

The goal of the focus group discussion was to understand the perspectives, perceptions, and prioritization of medication utilization review as a clinical service in POYC-MAS. Two resident doctors at Mater Dei Hospital who were exposed to POYC processes, three POYC pharmacists working in the entitlement unit, and a pharmacist from a community pharmacy that provides POYC services all took part in the conversation. Through group discussion, interprofessional collaboration was explored by addressing three main questions: 1) How should the prioritisation of drug utilisation review be designed? 2) What are the barriers to implementing drug utilisation review in POYC? 3) Given the barriers mentioned, what are the proposed interventions to address the barriers?

Based on the discussion, a tool was developed based on needs and feasibility in the entitlement unit ensuring drug risk minimisation while optimizing medicine access. The developed tool documents demographic profile, schedule V conditions, approved entitled medication, drug-related problems identified and its rationale, and the proposed intervention (Appendix 2).

Validation was performed on the designed tool to ensure its validity and usability. Two general practitioners, three pharmacists in POYC-MAS, and one academic pharmacist participated in content validation. The first developed tool was sent to the evaluators for review and suggestions. Further comments on the addition and deletion of contents of the tool were encouraged to the evaluators. Feedback from the participants were incorporated into the developed tool and revisions were sent for their approval. A validation form was provided where they can indicate their rating on the agreement or disagreement on the contents of the tool based on professional judgement.

2.5 Phase 2: Retrospective analysis

The developed tool was implemented in identifying drug-related problems through retrospective medication review of elderly patients with multiple conditions with at least ten entitled medications in oral, transdermal, inhalation, and ophthalmic dosage forms. For information extraction, the POYC Data Controller was provided with the established criteria. Patients' entitled medications and Schedule V conditions with assigned patient codes were supplied to the researcher in an electronic file by the data officer. From 14,005 patients' data generated according to criteria, 150 patients' (8% margin of error) were selected through random sampling. The guidelines used to classify drug related problems were: Improving Medicines and Polypharmacy Appropriate Clinical Tool (IMPACT)[7], Screening Tool of Older People's Prescriptions (STOPP) and

[7] National Health Servise (NHS) PrescQIPP. IMPACT - Improving Medicines and Polypharmacy Appropriateness Clinical Tool [Internet]. United Kingdom: NHS; 2020. [cited 2022 May 19]. Available from URL:http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Clinical_Guidelines/clinical_guidelines_front_page/PrescQipp_IMPACT.pdf

Screening Tool to Alert to Right Treatment (START) toolkit [8], and Polypharmacy Guidance, Realistic Prescribing[9], while Stockley's Interactions Checker was used to determine drug interactions.

2.6 Phase 3: Prospective risk assessment

The selection of expert panel was based on the desirability of including a wide variety of experts from the POYC scheme, who are all involved in the patients' medication management. Two community pharmacists and two family specialist medical doctors were on the panel, each with at least ten years of experience in daily patient care, including the POYC scheme. Community pharmacists that participate in the POYC programme are easy-to-reach healthcare providers who patients can inquire about medicine supply, side effects, and other drug-related questions. General practitioners are family specialists who see POYC patients for re-evaluation of treatments, either to renew previously prescribed treatments or to add a new one in limited circumstances.

Ten patients were selected from the 150-research sample size using the following criteria: patients who had the most common identified DRPs, which were drug interaction, adverse reactions, and unnecessary drug therapy issues; patients who have medications that are prescribed to at least 20% of the total research population; a

[8] National Health Service. STOPP START Toolkit Supporting Medication Review [Internet]. Cumbria: NHS;2016 [cited 2022 May 20]. Available from URL: https://www.valeofyorkccg.nhs.uk/seecmsfile/?id=3035&inline=1

[9] Scottish Government Polypharmacy Model of Care Group. Polypharmacy Guidance, Realistic Prescribing 3rd Edition [Internet]. Scottish Government. 2018. [cited 2022 Jan 15]. Available from URL: https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2018/04/Polypharmacy-Guidance-2018.pdf

proposed action plan for drug-related problems is at the prescriber level; and patients with a cardiovascular condition. Three drug-related problems were selected in each patient for prospective risk assessment. The explanation behind how the drug-related problem emerges was presented with outcomes and proposed interventions for the risk panel members to review.

For the panel members to have a universal standard in assessing each medication issue, a risk matrix table was provided with the "probability" and "consequence" ratings (Appendix 4). The “consequence” is the potential outcome of the drug-related problem, while “probability” is an estimate of the chance of an event or an incident happening, whether defined, measured, or determined objectively or subjectively.

The panel was given a total of 30 drug-related problems from 10 selected patients to assess risk by ranking both "probability" and "consequence" scores. After each of the drug-related problems had been rated, the probability and consequence ratings were transformed to risk scores on a scale of 1 to 5, denoting very low, low, moderate, high, and very high risk. Very low-risk drug-related problems require no treatment. Low risk results in minor drug-related problems requiring first aid. Moderate risk is DRPs requiring medical treatment. High risk is serious DRPs, which may require hospital treatment, while very high-risk DRPs can cause death and permanent disability (Kaya et al, 2019; Pascarella et al, 2021).

2.7 Data management and statistical analysis

A management plan for the research data was put together to determine the following: (a) demographic data (b) drug-related problems (c) risk assessment (d) data encoding and access (e) source of data (f) analysis of data.

For categorical data expressed as numbers and percentages, and continuous variables expressed as median, Microsoft Excel for MAC version 16.54 was utilized. The prioritization criteria, perceived barriers, and proposed interventions to overcome barriers were analysed using content analysis. The significant statements made during the interviews of the healthcare professionals were extracted and themes were developed from these core ideas. Descriptive statistics, specifically frequency and percentage were used to present the medication-related variables of the research population. Frequency and percentage were used also in determining the frequency of major therapeutic classes and in presenting the identified drug related problems.

The median risk scores in the risk assessment of drug-related problems were calculated using the probability and consequence ratings. The interquartile range was used to determine the participants' level of agreement on the risk scores.

Chapter 3

Results

3.1 Characterisation of drug utilisation review In POYC

The needs and obstacles in establishing a clinical review were determined based on the opinions and experiences of the focus group discussion members. The information is crucial in building a reasonable action plan for the POYC setting.

3.1.1. Perceived barriers in implementing drug utilisation review

Table 3.1 highlights the barriers extracted from the views of health professionals relative to the proposed drug utilisation review service. Five essential themes were identified, namely: limited access to patients' medical history; difficulty in the current POYC system; conflicting views among healthcare providers; communication constraints; lack of manpower; and medication reconciliation limitations.

Table 3.1. Perceived barriers in implementing drug utilisation review in POYC

Themes	**Core Ideas**
Limited Access to Patients Medical History	Lack of patient data access
	Limited to the information of patient's chronic entitlement
	Inability to obtain proof of their diagnosis
	No access to the patent's hospital history
Difficulty in the Current System	The system is not yet electronic
	The process is complicated
	Difficult to do clinical review against a criterion manually
	Entails a lot of work
	Time consuming
Conflicting Views Among Healthcare Providers	Doctors may have different viewpoints on the DRP findings
	When a patient is seen by several consultants, it might be difficult to know who to contact about a medication concern
Communication Constraints	The medical practitioner takes a long time to respond
	Some emails go unnoticed
Lack of Manpower	Insufficient pharmacists
Limitations on the medication reconciliation	Patient's private medications not disclosed
	Limited type of medicines to review

3.1.2. Perceived intervention on the barriers in implementing drug utilisation review

Interventions on the barriers to implementing the drug utilisation review are shown in Table 3.2. Additional manpower, an established drug interaction checker, full access to

patients' medical profiles, process simplification, and interprofessional collaboration are the five solutions discussed.

Table 3.2. Proposed action plans to the barriers identified

Themes	**Proposed Action Plans**
Additional Manpower	Addition of clinical pharmacists
	The entitlement unit's staff need training
Interactions checking tool	Provision of efficient and reliable drug Interaction checker
Comprehensive Access to Medical Profile	Comprehensive access to patient information like case summaries and laboratory results
	Vetting is possible of access to electronic notes
Simplification of Process	Automation
	Electronic system linking the pharmacy and the hospital
	Flagged systems
Interprofessional Collaboration	Emails with high priority should be communicated efficiently

3.1.3 Prioritisation of drug utilisation review

All respondents (n=6) agreed that the review should focus on the older population with diverse illnesses managed by several consultants. The majority (n=5) agree that the patients who can benefit from the medication review should have at least 10 POYC-eligible medications. According to the research respondents, dermatological conditions, rare diseases, and POYC equipment such as swabs, bandages, and catheters should be

excluded from the DUR requirements. All (n=6) acknowledged that the identifiable drug-related problems in the POYC are drug interaction, adverse drug reactions, drug duplication, unnecessary medication, and unclear dose, based on their professional experience.

3.2 Retrospective drug utilisation review

A total of 150 patient medication records from POYC database were reviewed using the developed tool (Appendix 2) and evidence-based guidelines.

3.2.1 Research population characteristics

Patient profiles investigated for drug-related issues were 60% male and 40% female. The vast majority of these patients are between 61 and 80 years old. The elderly population benefits from a routine medication assessment, especially if they are taking multiple treatments. Table 3.3 summarised the frequency of demographic profiles of the research subject.

Table 3.3 Patient's Demographic Data (N=150)

Characteristic	**Description**	**n (%)**
Gender	Male	90 (60)
	Female	60 (40)
Age	≤ 60	5 (3)
	61-70	49 (33)
	71-80	54 (36)
	81-90	36 (24)
	>90	6 (4)

3.2.2 Medication-related characteristics

For the number of medications prescribed per patient, 84% (n=126) of the research population had 10-15 medications applied by consultants approved by POYC-MAS while 23% had 16-20 medicines. Without proper guidance on the correct timing of taking multiple therapies, it will result in potential harm.

Multiple therapy was prescribed to manage different chronic conditions, and 81% (n= 122) suffered from hypertension, 58% (n= 87) had diabetes mellitus, and 53% (n= 80) were diagnosed with ischemic heart disease. Apart from cardiovascular illness, gastroesophageal disease affects 57% (n=86) of the study participants. The characteristics of medication-related factors obtained from the study are shown in Table 3.4.

Table 3.4 Medication-related variables (N=150)

Characteristics	**Category**	**Frequency (n, %)**
Number of medications per patient	10-15	126 (84)
	16-20	23 (15)
	21-25	1 (1)
Top 10 Disease Conditions	Hypertension	121 (81)
	Diabetes Mellitus Type 2	87 (58)
	Ischaemic Heart Disease	79 (53)
	Gastro-Oesophageal Reflux Disease	57 (38)
	Chronic Heart Failure	36 (24)
	Chronic Obstructive Pulmonary Disease	22 (15)
	Chronic Asthma	21 (14)
	Glaucoma	20 (13)
	Cardiac Arrhythmias	19 (13)
	Malignant Diseases	19 (13)
	Chronic Mood Disorders	18 (12)
	Unknown Disease	18 (12)

The distribution of 118 drugs prescribed in this study according to the pharmacological system is shown in Figure 3.1. The cardiovascular system accounts for 35% of medications, the nervous system for 14%, miscellaneous treatments such as vitamins and urinary system for 11%, the musculoskeletal system for 9%, the eyes, nose, throat, and gastrointestinal system for 7%, and infection control for 7%.

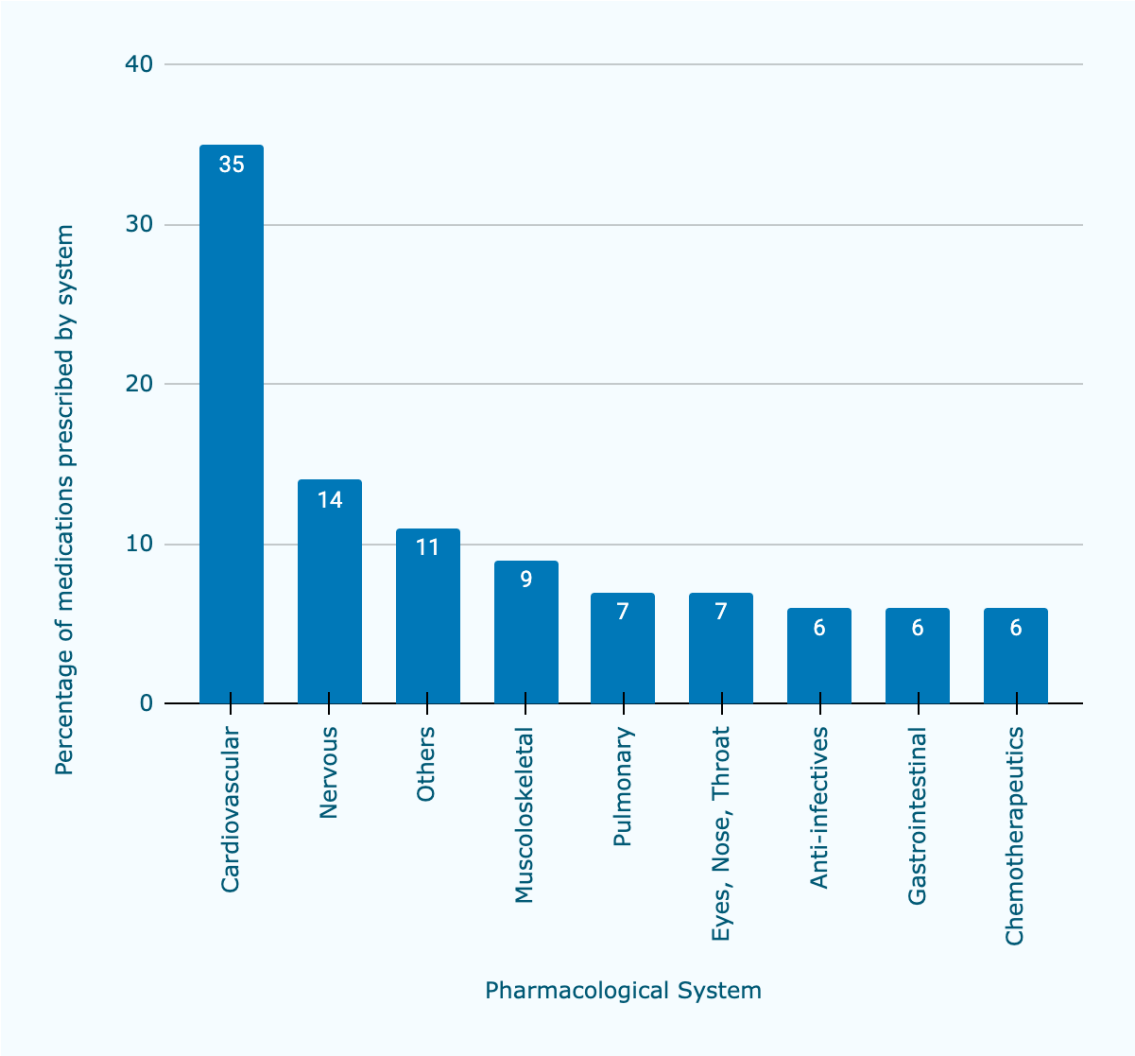

Figure 3.1. Medicines used according to pharmacological system (N=118)

Figure 3.2 shows how frequent the medications were prescribed to 150 patients in the study. The top 10 medications commonly prescribed were: aspirin (67%), amlodipine (61%), omeprazole (58%), metformin (55%), bumetanide (52%), perindopril (47%), atorvastatin (43%), gliclazide (41%), simvastatin (41%), amiodarone (33%), bendroflumethiazide (30%), and carvedilol (30%). Only omeprazole, among the

frequently used medications, is not used to manage a cardiovascular condition and endocrine comorbidities.

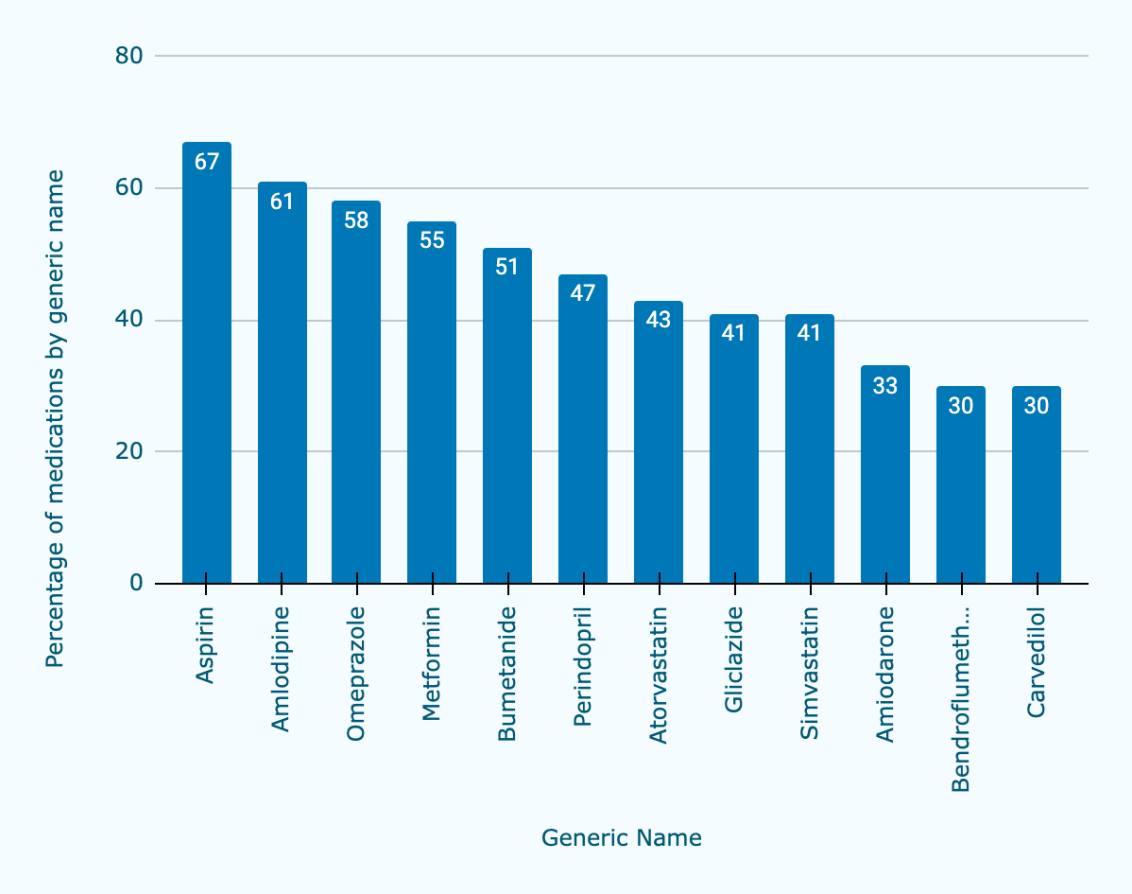

Figure 3.2 Medications frequently prescribed (N=118)

3.2.3 Drug-Related Problems

In the drug utilisation review, 1,088 different drug-related issues were identified and are described in Table 3.5. The top 5 medication issues were potential interaction between drugs (34%), risk for adverse drug reactions (22%), potentially unnecessary drug therapy (20%), adherence/patient centeredness (9%), and inappropriate duration of treatment

(6%). From the 369 potential drug interactions identified, 28% are major, 64% are moderate, and 28% are minor, according to Stockley's and Drugs.com interaction checkers.

Table 3.5 Drug-Related Problems Identified (N=1088)

Drug-Related Problems	**Frequency (n, %)**
Potential Interaction between drugs	369 (34)
Risk for Adverse Drug Reactions	233 (21)
Potentially Unnecessary drug Therapy	217 (20)
Adherence/Patient Centeredness	94 (9)
Inappropriate Duration of Treatment	66 (6)
Drug-patient precautions	57 (5)
Potential Drug-Disease Interactions	37 (3)
Therapeutic Duplication	14 (1)
Incorrect drug dosage	1 (0.09)

One of the most common major interactions that can result in elevated potassium levels in the blood is the use of spironolactone with valsartan. Hyperkalemia is a disorder caused by high potassium levels that can lead to kidney failure, muscle paralysis, abnormal heart rhythm, and cardiac arrest in extreme cases. Another DRP which can lead to a serious outcome is the use of co-administration of amiodarone and bumetanide. Because of their additive arrhythmogenic potential, co-administration of amiodarone and bumetanide, which can cause hypokalemia and/or hypomagnesemia,

can result in an increased risk of ventricular arrhythmias, including ventricular tachycardia and torsade's de pointes.

Amlodipine is among the medications commonly prescribed in this study that have common (≥1/100 to <1/10) undesirable effects of palpitations, flushing, shortness of breath, and visual disturbances. [10] Dizziness, vertigo, tinnitus, cough, gastrointestinal disturbances, muscle cramps, rash, and cough are all common adverse effects of perindopril, which is one of the most commonly used treatment in the study population. [11] Patients' potential adverse pharmacological effects will lead to poor adherence to therapy, especially for those who are fragile enough to experience the unwanted consequences.

The identified drug-related problems require intervention to ensure medication safety. In Table 3.6, the levels of proposed intervention for drug-related problems were described as being at the prescriber level and the patient level. Prescribers are either informed about minor drug issues or advised an intervention for other prescription problems that require immediate attention. Medication counselling on the monitoring required and the optimum time to take the medication are examples of recommendations at the patient level.

[10] Electronic medicines compendium (EMC). Summary of product characteristics - Amlodipine 10mg tablets. 2020 [cited 2022 May 23]. Available from URL: https://www.medicines.org.uk/emc/product/5702/smpc#UNDESIRABLE_EFFECTS

[11] Electronic medicines compendium (EMC). Summary of product characteristics – Perindopril 4mg tablets. 2020 [cited 2022 May 23]. Available from URL: https://www.medicines.org.uk/emc/product/5702/smpc#UNDESIRABLE_EFFECTS

Table 3.6 Level of Proposed Intervention to Drug-Related Problems

Proposed Intervention	Frequency
At prescriber level	806
At patient level	455

3.3 Prospective Risk Assessment

The data in Table 3.7 shows the risk assessment of the ten selected patient cases from the four panel experts, composed of two medical practitioners and two community pharmacists. The median risk scores for drug-related issues were 3, 4, and 5, indicating that the risks are moderate, high, and very high, respectively. The interquartile range (IQR) was determined using the median risk scores to measure the variability in the risk assessment scores of the identified drug-related problems among the panel experts. The IQR values for 28 of the 30 drug-related problems assessed were less than or equal to 1, indicating that the panel experts' risk assessment scores were in agreement. Only two computed IQRs are greater than 1, implying that the expert panels' risk assessment scores were varied.

Table 3.7 Drug related problem risk assessment

Drug-Related Problem	n	Median Risk Score	Interquartile Range
Potentially Unnecessary Drug Therapy	1	3	0.75
Risk for Adverse Drug Reactions	8	3-5	0.00-1.00
Potential Interaction Between Drugs	21	3-5	0.00-2.25

1 Very Low; 2 Low; 3 Moderate; 4 High; 5 Very High

Fifteen drug-related problems (N = 30) have a moderate risk, 10 have a high risk, and five have a very high risk. This research found drug-related issues, which were evaluated by a panel of experts to result in permanent disability or death if they happened. When hyperkalemic medicines like perindopril and spironolactone are given combined to patients with diabetes and severe renal impairment, they can cause life-threatening and fatal hyperkalemia within days to weeks of starting the combination treatment. By decreasing platelet aggregation, increasing bleeding time, and producing gastrointestinal lesions, aspirin, even in small doses, may increase the risk of bleeding in patients taking oral anticoagulants. Another DRP identified is the concomitant use of aspirin and warfarin. By decreasing platelet aggregation, increasing bleeding time, and producing gastrointestinal lesions, aspirin, even in small doses, may increase the risk of bleeding in patients taking oral anticoagulants. When diclofenac and spironolactone are taken together, it may cause an increased risk of acute renal failure and gastrointestinal bleeding. Diclofenac increases the risk of heart attack and stroke in patients with ischaemic heart disease, peripheral artery disease, cerebrovascular disease, and congestive heart failure. Perindopril, spironolactone, aspirin, and diclofenac are

medications easily accessed by POYC patients on a long-term basis, which requires a clinical review to not just provide medication as per protocol and formulary based approval but to consider medication safety in the process.

Chapter 4

Discussion

4.1 Drug utilisation review process

One essential part of maximizing universal health coverage is to secure patient safety. The involvement of a complex system, numerous procedures, and multiple healthcare professionals that comprise the health care delivery system provides both benefits and unavoidable hazards. Every year, a significant number of patients are harmed or die because of unsafe health care, resulting in a high public health burden worldwide. [12] Provided that medications are the most convenient route to manage health conditions, efficient identification and prevention procedures of drug-related problems are fundamental in contributing to safe and effective healthcare for the majority. It is valuable that a health care setting instigates an essential step to expand the existing health services for suitable polypharmacy management.

POYC's excellent commitment to its service towards provision of pharmaceutical service and patient-centric service continues to advocate for improvement. In the 2019 technical report on medication safety in polypharmacy, the World Health Organization (WHO) has challenged governments and key stakeholders to prioritise drug safety in transitions of care, polypharmacy, and high-risk scenarios as part of the Global Patient Safety Challenge: Medication Without Harm. In the WHO report, formalized processes, workforce capacity and competence, engaging with patients and families, enhancing information quality and availability, and measurement are some of the major features

[12] World Health Organization. Medication Safety in Polypharmacy. WHO; 2019. [cited 2022 Feb 7]. Available from URL: https://apps.who.int/iris/rest/bitstreams/1235792/retrieve

of leadership and improvement programmes identified to promote pharmaceutical safety practices. [13]

Structured drug utilisation review as an additional POYC service may increase vigilance for preventable drug-related issues, particularly given the traditional practice of prioritizing disease management on a single disease approach within the polypharmacy reality. From previous studies conducted in Malta, drug utilisation review as a clinical service has gained interest in reducing medicine wastage (Cassar, 2020), treatment delays (Ayran, 2021), and preventable drug-related issues (Farrugia et al, 2011; Magno, 2021). Although risk-reduction strategies were available for clinical use, it was vital that the DUR tool developed for POYC be appropriate for its unique setting, in which medications were vetted through a government formulary list before being approved. Before a medication is approved as a free supply, the process can include a clinical component. Reviewing existing mitigation strategies contributes to the development of a risk minimization tool suitable for the POYC setting.

Barriers were perceived in putting forward drug utilisation review as a clinical service in POYC. One of the barriers that surfaced in the discussion is the limited access to patient medical history, evidence of diagnosis, hospital discharge history, and out of pocket expenditure on medicines. This data limitation prevents the pharmacist from gathering clinical evidence such as laboratory results and case summaries, which are important

[13] World Health Organization. Medication safety in transitions of care [Internet]. WHO; 2019 . [cited 2022 Feb 7]. Available from URL: https://www.who.int/publications/i/item/WHO-UHC-SDS-2019.9

components of identifying medication-related issues in a comprehensive clinical review. The current POYC system's data accessibility limitations and lack of electronic processes are obstacles to delivering patient care. As a consequence, doing a medication review requires a lot of work and time to execute requiring additional manpower. While it is true that the data required by pharmacists for clinical review is scarce, having the availability of digital records of the patient's medications is a major motivating component, as is having access to previous research works (Tuula et al, 2021). Drug utilisation review can be implemented as a clinical service in POYC with resources such as digital access to patient profiles, a drug interaction checker, full access to evidence-based guidelines, and an appropriate medication review tool with the necessary manpower. Without these resources, time spent on clinically reviewing drugs will be consuming, resulting in treatment delays.

A drug utilisation review's significant findings must be communicated to medical practitioners. This can be a problem if various specialists treating the patient have opposing viewpoints on the identified medication-related condition, causing therapy to be delayed. In the focus group conducted in this study, it came up that while some medical practitioners are quick to reply, others take time to send a communication response to resolve medication inquiries. Donovan et al (2018) described interprofessional care as care provided by a group of healthcare professionals with complementary expertise and a consideration of the unique contribution of other team members as collaborators in achieving a common goal. For sustainable care delivery, the establishment of healthcare collaboration requires assistance from the larger

organisational framework to enable professionals to work intensively together for reciprocal consultations and interprofessional meetings on a regular basis (van Dijk-de Vries et al, 2017). To optimise the clinical findings in the DUR, consultants and general practitioners participating in the POYC scheme must support pharmacists by establishing efficient communication as a team working on the goal of improving the delivery of care to patients.

Pharmacists are in an ideal position to undertake a medication review for a large number of patients with chronic illnesses (Okoro & Nduaguba, 2021). The clinical review service could be launched in POYC by training and adding pharmacy staff capable of performing the clinical review, supplemented by good access to patient information such as case summaries and laboratory results; simplifying the system by making it electronic and user-friendly; and encouraging interprofessional collaboration. In addition to the pharmacy administrative tasks currently performed by pharmacists in POYC, the drug utilisation review allows them to take on clinical roles. When a consultant applies a new treatment for a patient to POYC, the application is examined against the government formulary list. DUR gives an opportunity to integrate patient-centered strategies into protocol-based evaluation, aiming for medication safety upon approval of the entitlement of free medications. In the study of Liou et al, (2021), patients improved in identifying their health state, caring for themselves, following their doctor's orders, and contentment with the pharmacist's clinical service, as well as a considerable drop in the number of DRPs, according to a pharmacist-led study in an aged population. When compared to usual care, a pharmacist-led educational intervention resulted in more

prescriptions for inappropriate medication being discontinued in the senior population (Martin et al, 2018).

This research demonstrates that drug utilisation review is an essential service for patients who benefit from the POYC scheme, particularly the elderly with a cascade of conditions who are on multiple medications. POYC is a platform to consider for a clinical review on whether a new medication applied for an entitlement can cause drug-related problems like adverse effects or drug interactions when added to other existing treatments. The DUR is an advantageous process since consultants can continue to apply for new prescriptions without having to withdraw past treatments. As a result of stockpiling on approved entitlements, patients and pharmacists who dispense free medications may become confused between current therapy and discontinued treatment. The patient may mishandle the medicines or distribute them with others, providing a further risk. A medical condition or comorbidity might worsen as a consequence of poor disease and drug management.

During the retrospective drug utilisation review, the majority of the elderly research population were prescribed 10–15 medications, resulting in polypharmacy. Pharmaceutical errors, incorrect medication prescribing, potential adverse effects and interactions, medication-related admissions, poorer quality of life, increased mobility challenges, and higher mortality have all been linked to polypharmacy (Halli-Tierney et al, 2019; Nabhanizadeh et al, 2019). Due to age-related pharmacodynamic and pharmacokinetic changes such as reduced first-pass metabolism, bioavailability, rise in

excess fat, decline in body water, and lean body mass, the elderly population is most at risk of severe effects from drug-related disorders (Shi & Klotz, 2011; Dagli & Shama, 2014). Consequently, it is critical that physicians or other health care providers pursue discussions about any medication-related difficulties in older persons on a regular basis, as older people can swiftly change how they handle their medications (Drenth-van et al, 2020). Pharmacists can participate in medication discussions and offer prescribers additional information regarding the efficacy and safety of treatment options planned for disease management.

Hypertension, diabetes mellitus type 2, and ischemic heart disease were the most commonly diagnosed conditions among the study participants. Cardiovascular diseases (CVDs) are the largest cause of death worldwide, accounting for 17.9 million fatalities in 2019, or 32% of all deaths worldwide. At least 50% of adults with cardiovascular risk should acquire medication therapy and counseling to avoid heart attacks and strokes, according to the WHO Global Action Plan for Prevention and Control. [14] Participation to realize this goal is through medication review and evidence-based interventions communicated to medical practitioners as an important step to proceed with patient education regarding disease management. For example, the goal of therapy in patients with atrial fibrillation (AF) is to forestall stroke, which can be strengthened through drug use review. As per the findings, some people at risk of stroke may not be taking anticoagulants as recommended by the National Institute for Health and Care Excellence

[14] World Health Organization. Cardiovascular diseases (CVDs). WHO; 2021 [cited 2022 Mar 11]. Available from URL: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)#:~:text=Cardiovascular%20diseases%20(CVDs)%20are%20the,%2D%20and%20middle%2Dincome%20countries.

(NICE). In an audit done by National Institute for Health and Care Excellence, nearly 6,000 strokes may be avoided each year if everybody with AF was treated properly with anticoagulants.[15] Pharmacist education on illnesses and drugs can help patients with cardiovascular disease live better. According to a study published in 2020 by Alshehri, pharmacists' involvement as healthcare practitioners in the management of patients with hypertension, diabetes, and dyslipidemia in primary care might considerably lower medical risk factors for cardiovascular disease incidents. Since cardiovascular treatments are being prescribed to a large population in this study, it is an avenue for pharmacists in POYC to review their treatments for appropriateness and potential issues.

Other than deprescribing unnecessary medication, other drug related issues need to be looked into to minimise their risk. The most common drug issues identified in the study were drug interactions, adverse drug reactions, and unnecessary drug therapy. These drug-related problems can be identifiable and preventable (AlAzmi et al, 2019). Hence, the relevance of conducting drug utilisation reviews as a mitigation strategy to avoid and limit the occurrence of medication issues caused by high-risk treatments and polypharmacy is highlighted by this study.

Distinguishing the clinically relevant drug interactions is a requisite to patient safety. Drug interactions may be responsible for 1% of all hospitalizations in the general public

[15] National Institute for Health and Care Excellence. NICEimpact cardiovascular disease prevention. NICE;2018 [cited 2022 Mar 11]. Available from URL: https://www.nice.org.uk/media/default/about/what-we-do/into-practice/measuring-uptake/nice-impact-cardiovascular-disease-prevention.pdf

and 2–5% of hospital admissions in the older adults (Létinier et al , 2019). In this study, drug interaction is at the top of the list among the drug issues. This is one of the result of polypharmacy, especially when patients have issues comprehending the long list of medications they are taking. In this research, an example of a positive drug interaction may occur from the numerous antihypertensive medications prescribed to lower abnormally high blood pressure. However, patient education is essential on the signs of hypotension, such as dizziness, fatigue, and blurred vision, for them to be aware when to seek medical advice. In this manner, a patient keeps track of their response changes to therapy. Some treatments, when taken together, are known to cause a negative interaction, such as the risk of digoxin toxicity when digoxin is taken with amiodarone. Nausea, anorexia, visual abnormalities, slow pulse, or irregular heartbeats are all dangerous and life-threatening manifestations of digoxin toxicity. [16] When fluvoxamine is taken at the same time as antiplatelet medications like aspirin, there is a risk of bleeding (Labos et al, 2011). In this scenario, Tsai et al (2011) highlight that it is critical to stress the need to consider gastroprotectants like omeprazole, especially for vulnerable individuals like the elderly who have a history of gastrointestinal bleeding. Carpenter et al (2019) describes that minimizing the number of drugs prescribed, re-evaluating therapy on a regular basis, considering nonpharmacologic options, monitoring for signs and symptoms of toxicity or effectiveness, adjusting medication dosages when indicated, and adjusting administration times are all helpful strategies that a pharmacist can implement to reduce the risk of drug-drug interactions.

[16] Drugs.com. Drug Interaction Report – Amiodarone, Digoxin. 2022 [cited 2022 Jun 4]. Available from URL: https://www.drugs.com/interactions-check.php?drug_list=167-0,883-0&types%5B%5D=major&types%5B%5D=minor&types%5B%5D=moderate&types%5B%5D=food&types%5B%5D=therapeutic_duplication&professional=1

Potential drug interactions are evaluated in this study based on the list of approved entitlements rather than the patient's actual used medications. In some cases, not all entitled medications are used by patients; some are applied by the consultant, so when a condition progresses, the change in therapy can be initiated. The DUR highlights the value of not taking medications together due to unfavourable health implications, not just for the prescriptions taken by the patient, but for the entire list of entitled medicines. The findings of the DUR are applicable to guide patients to the untoward effects of medications requiring close monitoring and as a caution for medications not safely taken together if the whole list of entitlements is used. As a result, health hazards associated with drug-related problems are prevented.

Adverse drug reaction (ADR) is a common medication issue that results in harmful events after medication use. Certain ADRs, according to Kaufman (2016), are predictable as responses that can be predicted based on a drug's pharmacology. Examples of preventable ADRs documented in this research were the cumulative effects of medications causing hypoglycemia, hypotension, hypokalemia, hypomagnesaemia, and constipation. Others, such as anaphylaxis, are classified as unpredictable, which refers to reactions that deviate from the known pharmacology of a drug and are associated with high morbidity and mortality. Many can be avoided with proper planning and monitoring by using early risk mitigation strategies. Age, the variety of medications and illnesses, the level of the health care facility, the history of adverse reactions, and the type of medicine all had an impact on the severity of ADR (Yan et al, 2021). ADRs

expanded from 13% in people taking two drugs to 58% in those taking five, and 82% in people taking seven or more (Davies & O'Mahony, 2015).

To avoid an ADR, two main actions can be used: recognise the segment of patients who are likely to be vulnerable to the adverse effect and alter adequate treatment, and ensure the treatment plan ameliorates any potential adverse effects (Coleman & Pontefract 2016). When there is an oversight in detecting an ADR, a prescribing cascade can occur, resulting in a continued risk of ADR from the culprit drug as well as extra risk from the newly given drug. The prescription of an anticholinergic medication to alleviate the extrapyramidal symptoms of an antipsychotic medicine is an illustration of this practice. Anticholinergic medicine raises the risk of cognitive decline, orthostatic hypotension, impaired vision, constipation, and urine retention, all of which can lead to falls, delirium, and cognition and functional loss (Lavan & Gallagher, 2016). A diligent examination of the risks and benefits of medications can be used to prevent and detect harmful effects from medicines throughout the life cycle of a medicine, from pre-approval to patient use. [17] This study's findings account for 21% (n=228) of potential adverse drug reactions, necessitating patient education on how to recognise them and what to do if they occur.

Medication concerns such as unnecessary therapy, drug duplication, incorrect dose dosage, and unnecessary therapy requires intervention. Prescribers can be informed

[17] World Health Organization. Safety of medicines – adverse drug reactions. [cited 2022 Mar 12]. Available from URL: https://www.who.int/docs/default-source/medicines/safety-of-medicines--adverse-drug-reactions-jun18.pdf?sfvrsn=4fcaf40_2

about these measures to enable them to develop a better plan through interprofessional collaboration. Patients can be informed about interventions through patient counselling, which can enable them to understand their disease and therapy by involving them in drug management. Abdel-Latif (2017); Dalton et al (2022) mentioned that the attributes of the intervention, the underpinning drug-related problem, patient factors, pharmacist characteristics, and the prescriber's medical specialty, as well as developing partnerships, interdisciplinary team communication, and the healthcare setting, all influenced acceptance of the recommendations to address a drug-related problem. Hecht et al (2016) described that pharmacist training is a salient point to consider to enhance skills and knowledge in evidence-based medicine. POYC pharmacists will need appropriate procedures to be used for training development, piloting, assessment, reporting, and implementation as support in the future transition to providing clinical service since the current pharmacist's role focuses on the administrative and protocol-based duties.

Drug-related problems pose a different level of risk. The danger of not having any comprehensive risk management plans to hamper potential drug issues gives rise to long-term effects, compromising patient care and financial burden. Risk management plan is critical for avoiding drug errors and can play a key role in quality assurance policies (Oltean, 2018). In healthcare, risk analysis entails considering the sources of risk, their consequences, and the likelihood that the implications may happen to patient safety, healthcare providers, and the institution, in order to identify minor acceptable clinical risks from unacceptable major risks (Pascarella et al, 2021). Detecting the level

of the hazard potentially caused by a drug related problem means looking ahead to its possible consequences in potentially causing health hazards. By doing a risk assessment, more appropriate actions can be taken to reduce risks and choices made in the event of unfavourable outcomes (Kaya et al, 2019). In this study, after the risk had been identified, a clinical intervention was planned to be proposed to the prescribing medical doctor or as a medication counselling for the patient. Even though the interventions in this study were not reported, if the interdisciplinary procedure is practised in the future, it will safeguard patient safety.

Prioritising a drug problem that must be treated immediately may be given top priority. Drug issues may result in low, moderate, or high risk. Beales & Tulloch (2013) described patients aged 75 years old as being in four risk categories due to the severity of their chronic conditions, impairments, and socioeconomic challenges. Patients with low risk produces medical problems that are neither important nor progressive; medium risk has an impact on the patient's day-to-day life, but non-medical issues must be identified. High risk can lead to impairment and non-medical issues, which can have a substantial impact on daily life and put patients at risk of being institutionalized. Very high-risk patients are frail or severely impaired people who have a lot of medical or non-medical problems and are on the point of needing institutional care. This study's risk assessment data demonstrates that drug-related problems are moderate to extremely high risk, necessitating close attention to care, to avoid lost time and serious outcomes like hospitalisation and disability.

According to a 2017 study by Lin et al, antipsychotics were shown to have the highest risk of unplanned hospitalisation, followed by NSAIDs, anticonvulsants, diuretics, benzodiazepines-hypnotics, antidepressants, and antiplatelets. In a study published in 2021 by Huang et al, five high-risk medication patterns were found, including renin-angiotensin-aldosterone system (RAAS) inhibitors, RAAS inhibitors, mental health drugs, central nervous system (CNS) drugs, and antithrombotic clusters, especially among the elderly population. Medications have the potential to cause harm when two or more interacting medicines are used together or when inappropriate medications are prescribed to individuals with particular risk factors such as organ damage or co-morbid conditions. Early detection methods, such as drug utilisation reviews, may have a positive clinical consequence on medicine use. The DUR is not intended to create a hostile situation between pharmacists and doctors; rather, it is a practise that encourages teamwork that puts patient safety first.

4.2 Limitations of the study

Patient cases for risk assessment were based on the top three most commonly identified drug-related problems, making this criteria prone to rater bias by eliminating the chance of drug-related problems with low risk to be assessed. Although the types of drug-related problems and interventions were developed, these were communicated to the panel experts for assessment and not to the prescribing medical practitioner.

The clinical drug utilisation review was carried out only for older people who have at least 10 prescribed medications. The established criteria may have missed other patients who could have benefited from the drug utilisation review. The study used retrospective data created by the POYC data officer, and it was considered that the accuracy of the drug review was restricted solely by the priority criteria and the retrieval time of information from the POYC database.

4.3 Recommendations for future study

Future research could explore evaluating the clinical service's application in POYC-MAS by piloting the drug use review using the developed tool in a real-time setting. To assess the acceptance and impact of the clinical service given by pharmacists, proposed treatments for the detected drug-related problems should be communicated to the prescribing physician and the patient.

Autoimmune diseases and other chronic conditions, diverse age groups prescribed at least 5 medications, and high-risk treatments can all be considered as clinical review criteria in future research to generate more solid and strong data.

To establish and obtain stakeholder support for future research on the digitalization of drug utilisation reviews, including full access to patient medical information, an interaction checker, and clinical guidelines, as well as to quantify the impact of therapeutic interventions.

4.4 Conclusion

The study explored the opportunity for POYC pharmacists to offer a clinical service through a drug utilisation review. The panel of experts expressed that the clinical review is not just important but essential for a wide array of patients. Despite the barriers discussed, healthcare professionals had a positive outlook that the pathway to patient-centred service is feasible and could be an addition to the POYC services. This study revealed that having access to medical records of patients, simplification of the systems, additional manpower, and enhancement of interprofessional collaboration contribute to improving outcomes from POYC-led drug utilisation review in the future.

Considering the data gathered in the focus group discussion, a research tool was developed to be used in the drug utilisation review feasible to the POYC-MAS setting as a risk minimisation strategy. The review was performed through the use of updated clinical guidelines established by different organisations that constantly promote services that focus on medication safety and efficacy.

The result of the risk assessment from selected patient cases showed that the drug-related problems project moderate to high risks requiring clinical interventions. The risk rating scores of the panel of experts, which included medical practitioners and pharmacists, are mostly in agreement. POYC, as a healthcare unit, requires a transition from protocol and formulary-based services to clinical and patient-centered services.

Through the retrospective review, results showed that the majority of the research population were experiencing chronic cardiovascular conditions with comorbidities, hence the rationale behind the use of multiple medications. This demonstrates the importance of the medication review to assess and determine the interventions necessary for identified drug-related problems.

In POYC, a drug utilisation review is a clinical intervention that protects patients from prescription risks like adverse drug responses, drug interactions, and unnecessary therapy. The clinical review provides an opportunity for pharmacists to execute patient-centred roles that improve prescribing process results, such as polypharmacy reduction, and confirms that medications are appropriate for managing patients' diseases. When deprescribing is optimised, a patient requires fewer medications, resulting in improved medication adherence and cost savings for the healthcare system. The introduction of a POYC-led drug utilisation review at entitlement phase relies on communication with prescribers and collaborative care practices.

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Appendices

Appendix 1

FREC Approval Letter

L-Università ta' Malta

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Ref No: FRECMDS_2021_120

18 June 2021

Ana Lou Grace Manluyang
25 Mason, Flat 1
Triq Ganu
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Malta

Dear Ms Manluyang,

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

Risk Minimization Strategies Through Drug Utilization Review

The Faculty Research Ethics Committee is granting ethical approval for the above-mentioned application reviewed on 1 June 2021.

Yours sincerely,

Professor Pierre Mallia
Chairman
Faculty Research Ethics Committee

Appendix 2

Developed Research Tool

FORM 1. Drug Utilization Review (DUR)

Date of Evaluation	
Patient Identifier	
Gender	
Age	

CURRENT MEDICATION

	Schedule V Conditions	Entitled Medication	Frequency
1			
2			
3			

DRUG RELATED PROBLEM

Drug Related Problem	Mechanism of DRP	Proposed Intervention/s

PROPOSED INTERVENTION

1. At prescriber level
    - 1.1 Prescriber informed only
    - 1.2 Prescriber asked for information
    - 1.3. Intervention proposed to prescriber
    - 1.4 Intervention discussed with prescriber
2. At patient level - patient/family member counselling or written information provided
3. At drug level - changes on drug dose, formulation
4. Other specific interventions

Remarks :

_____

_____

Appendix 3

List of Drug Related Problems

LIST OF DRUG RELATED PROBLEMS

Drug Related Problems	**Description**
Drug-patient precautions	Gender, age, or organ related precautions
Potential Interaction between drugs	Potential drug interaction
Risk for Adverse Drug Reactions	Single or cumulative toxicity
Potential Drug-Disease Interactions	Drugs that are harmful in a condition and vice versa
Potentially Unnecessary drug Therapy	Unclear or Unconfirmed Indication for drug
Therapeutic Duplication	Multiple medications for the same indication or purpose without a clear distinction
Inappropriate Duration of Treatment	Treatment duration too short or too long
Incorrect drug dosage	Dose too high or too low
Adherence/Patient Centeredness	Self-Administration Check (Cognitive and technical)

Appendix 4

Risk Assessment Matrix

RISK ASSESSMENT

PROBABILITY SCORE		CONSEQUENCE SCORE				
		1 Negligible	**2 Minor**	**3 Moderate**	**4 Major**	**5 Catastrophic**
		Minimal injury requiring no or minimal intervention or treatment	Minor injury or illness requiring minor intervention	Moderate injury requiring professional intervention	Major injury leading to long term incapacity/disability	Death or multiple permanent injuries or irreversible health effects
1 Rare	May happen only in exceptional circumstances	1	2	3	4	5
2 Unlikely	Could happen some time	2	4	6	8	10
3 Possible	Might occur occasionally	3	6	9	12	15
4 Likely	Will probably occur in most circumstance	4	8	12	16	20
5 Almost Certain	Expected to occur in most circumstances	5	10	15	20	25

RISK GRADING COLORS				
1-2 Very low	3-4 Low risk	5-12 Moderate Risk	15-16 High Risk	20-25 Very high risk

Risk Rating Interpretation

Very low risk: Drug related problem requiring no treatment or first aid
Low risk: Minor drug related problem, first aid only required
Moderate risk: Drug related problem requiring medical treatment and some lost time
High risk: Serious drug related problem, hospital treatment required
Very high risk: Death or permanent disability

Appendix 5

Patient Cases for Risk Assessment

10 PATIENT CASES FOR RISK ASSESSMENT

Patient	Medicine Involved	Drug Related Problem
1	Valsartan, Spironolactone	Increase the risk of hyperkalaemia, which if severe may be life-threatening, particularly in those with diabetes and/or renal impairment.
	Aspirin, Fluvoxamine	The bleeding risk associated with antiplatelet drugs such as might be further increased by the concurrent use of an SSRI.
	Fenofibrate, Atorvastatin	Both medications cause rhabdomyolysis; these might be additive on concurrent use.
2	Amlodipine, Carvedilol, Perindopril, Doxazosin	Blood pressure may sharply reduce when calcium-channel blockers, beta-blocker, ACE inhibitor are first given to patients already taking alpha-blockers and vice versa.
	Omeprazole	PPIs should be reviewed 4-8 weeks after starting a treatment and discontinued where appropriate.
	Bumetanide, Digoxin	Hypokalaemia, which can be caused by potassium-depleting diuretics such as loop diuretics, increases the toxicity of the digitalis glycosides.
3	Levodopa, Olanzapine, Quetiapine	Some antipsychotics have dopamine antagonist actions which would be expected to inhibit the efficacy of LEVODOPA. Some evidence suggests that levodopa might antagonise the effects of antipsychotics. OLANZAPINE, QUETIAPINE causes deterioration in motor function in Parkinson's disease.
	Bumetanide, Sabutamol, Olanzapine	BUMETANIDE, SALBUTAMOL can cause hypokalaemia, increasing the risk of torsade de pointes, which might be additive with the effects of OLANZAPINE.
	Atenolol, Salbutamol	Cardioselective beta-blockers (ATENOLOL) can sometimes cause acute bronchospasm in patients with asthma but they do not generally inhibit the bronchodilator effect of beta-agonist bronchodilators (SALBUTAMOL).
4	Calcium lacatate, Bendrofluazide	Hypercalcaemia and possibly metabolic alkalosis can develop in patients given moderately large amounts of CALCIUM with or without high doses of vitamin D if they are also given a THIAZIDE.
	Perindopril, Spironolactone	The concurrent use of ACE inhibitors and potassium-sparing diuretics increases the risk

		of hyperkalaemia, which if severe may be life-threatening, especially in those with diabetes and/or renal impairment.
	Naproxen, Aspirin	Non-selective NSAIDs might antagonise the antiplatelet effects and reduce the cardioprotective effects of low-dose ASPIRIN. Concurrent use increases the risk of gastrointestinal bleeds.
5	Aspirin, Warfarin	Low-dose ASPIRIN (75 to 325 mg daily) increases the risk of bleeding when given with WARFARIN. High doses of aspirin (4 g daily or more) can also increase prothrombin times in patients taking warfarin.
	Carvedilol, Salbutamol	Non-selective beta blockers (CARVEDILOL) might oppose the bronchodilator effects of beta-agonist bronchodilators (SALBUTAMOL) resulting in serious and life-threatening bronchospasm.
	Salbutamol, Bumetanide	Beta-agonists (SALBUTAMOL) can cause hypokalaemia. This can be increased by other potassium-depleting drugs such as loop diuretics (BUMETANIDE). In severe cases the risk of serious cardiac arrhythmias could be increased
6	Diclofenac	Risk of exacerbation of hypertension and heart failure
	Diclofenac, Spironolactone	NSAIDs (DICLOFENAC) may possibly antagonise the antihypertensive and/or diuretic effects of SPIRONOLACTONE, and may also increase the risk of acute renal failure and hyperkalaemia. Concurrent use may increase the risk of gastrointestinal events (e.g. gastrointestinal bleeding).
	Diclofenac, Aspirin	Non-selective NSAIDs (DICLOFENAC) might antagonise the antiplatelet effects and reduce the cardioprotective effects of low-dose ASPIRIN. Concurrent use increases the risk of gastrointestinal bleeds.
7	Amiodarone, Simvastatin	Myopathy and rhabdomyolysis have been reported in patients taking AMIODARONE and SIMVASTATIN
	Amiodarone, Warfarin	AMIODARONE increases the anticoagulant effects of WARFARIN.
	Amiodarone	AMIODARONE is associated with multiple toxicities (thyroid, pulmonary, QT prolongation).

8	Ondansetron, Fluconazole	Both ONDANSETRON and FLUCONAZOLE have some risk of prolonging the QT interval, which might lead to the potentially fatal torsade de pointes arrhythmia. Dangerous QT prolongation might occur if they are used together.
	Fluconazole, Lenalidomide	Cases of rhabdomyolysis have been reported in patients given ATORVASTATIN FLUCONAZOLE and LENALIDOMIDE.
	Dexamethasone, Ondansetron, Fluconazole	DEXAMETHASONE can cause hypokalaemia, increasing the risk of torsade de pointes, which might be additive with the effects of ONDANSETRON and FLUCONAZOLE.
9	Amiodarone, Carvedilol	The concurrent use of AMIODARONE and a beta blocker (CARVEDILOL) has led to hypotension, bradycardia, ventricular fibrillation and asystole in a few patients. Amiodarone might inhibit the metabolism of carvedilol, which might be a factor in the interaction. Beta-blockers can cause hypokalaemia, increasing the risk of torsade de pointes, which might be additive with the effects of amiodarone.
	Amiodarone, Digoxin	AMIODARONE can double DIGOXIN levels. Some individuals may show even greater increases. Synergistic effects on heart rate and AV node conduction are also possible, and arrhythmias may occur with concurrent use.
	Carvedilol	Beta blockers (CARVEDILOL) might also mask some of the warning signs of hypoglycaemia.
10	Perindopril, Valsartan, Spironolactone	The concurrent use of ACE inhibitors (PERINDOPRIL), angiotensin II receptor antagonists (VALSARTAN) and potassium-sparing diuretics (SPIRONOLACTONE) increases the risk of hyperkalaemia, which if severe may be life-threatening, especially in those with diabetes and/or renal impairment.
	Aspirin, Warfarin	Low-dose ASPIRIN (75 to 325 mg daily) increases the risk of bleeding when given with WARFARIN.
	Salbutamol, Beclomethasone, Bumetanide, Prednisolone	SALBUTAMOL, BECLOMETASONE, BUMETANIDE, PREDNISOLONE can cause hypokalaemia, increasing the risk of torsade de pointes, which might be additive with the effects of AMIODARONE.

Appendix 6

List of Publications

Submitted to the 80th FIP World Congress of Pharmacy and Pharmaceutical Sciences

Title: Risk Minimisation Strategies Through Drug Utilisation Review

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Background information: The national pharmaceutical service in Malta provides free medicines and medical devices to outpatients through 219 private community pharmacies. Approval of free entitlement to medicines through the national service provider prioritises meeting pharmacy administrative processes. Clinical services during the entitlement review will benefit patients, ensuring treatment continuity across the healthcare system.

Purpose: To characterise the process of pharmacists' review at the national pharmaceutical service entitlement unit and include a risk-minimization strategy through a pharmacist-led drug utilisation review (DUR).

Method: A focus group discussion was organised to understand needs, advantages, barriers, experiences, and prioritisation of a clinical review process within the pharmaceutical service. A Drug Utilisation Review tool feasible for the setting was developed and validated by two medical practitioners, two national pharmaceutical service pharmacists, and one academic pharmacist for practicality. Subsequently, the tool was applied retrospectively to records of 150 patients (60% male, 40% female) entitled to at least 10 medications for various diseases managed by multiple medical practitioners to identify drug-related problems (DRPs). The risk of identified drug-related problems was assessed for 10 selected patient cases by a panel of pharmacists and medical practitioners using the matrix table with the "probability" and

"consequence" risk ratings on a scale of 1 to 5, indicating very low, low, moderate, high, and very high risk respectively. Very low-risk drug-related problems require no treatment. Low risk requires self-care, moderate risk is DRPs requiring medical treatment, high risk may require hospital treatment and very high-risk DRPs cause death and permanent disability. "Consequence" is the potential outcome of the drug-related problem, while "probability" is an estimate of the chance of an event or an incident happening.

Results: One hundred and fifty patients with multiple diseases and/or healthcare providers and entitled to at least 10 drugs were identified for prioritisation in the DUR process established through the focus group discussion. From the DUR exercise, 84% (n=126) had 10–15 entitled medications, with aspirin (67%), amlodipine (61%), omeprazole (58%), metformin (55%), bumetanide (52%), and perindopril (47%) as the most frequently prescribed medications. Hypertension (81%), diabetes mellitus type 2 (58%), and ischaemic heart disease (53%) were the top medical conditions identified. Among the 1,088 DRPs identified, 34% were potential drug interactions, 21% were increased risk of adverse drug reactions, and 20% were potentially unnecessary drug therapies. The median risk scores for 30 drug-related problems from 10 patient cases were 3, 4, and 5, respectively, suggesting moderate, high, and extremely high medication risk requiring medical intervention.

Conclusion: The developed DUR tool provides for a systematic patient-centered pharmacist intervention during the national pharmaceutical service formulary-based entitlement appraisal.

Topic area: Social and Administrative Pharmacy Section