Optimisation of Medication in Older Persons

Tiziana Fenech Caruana

submitted in partial fulfilment of the requirements of the

Degree of Doctorate in Pharmacy

Department of Pharmacy

University of Malta

2021

Dedication page

I dedicate this work to my family, my fiancé,

and the Almighty God.

Acknowledgement Page

I would like to thank:

- My supervisors: Head of Department Professor Lilian M. Azzopardi and Dr Marise Gauci for their constant guidance and advice throughout all phases of this research

- All the academic staff at the Department of Pharmacy for always being so inspirational and motivating in my studies

- The medical doctors, community pharmacists and patients involved in this research for being cooperative during the preparatory and data collection stages.

- Professor Liberato Camilleri for his help with the statistics

- My colleagues at Milia's Pharmacies. Special thanks goes to my employers Ms Arlette Falzon Seychell and Mr Owen Falzon for always being supportive and so accommodating in my timetable allowing me to juggle both work and study life.

- My father who has always provided me with his assistance and technical support throughout the research

- My parents Mario and Felicienne, sisters Miriana and Valentina, and fiancé Gabriel who have without a doubt shown me unending support and love without which I would not have reached this stage of my studies.

Abstract

Optimisation of medication in older patients is challenging and explicit criteria assist in the identification of pharmaceutical care issues enhancing pharmacist intervention. The aim of the research was to assess the feasibility and applicability of clinical tools adopted by pharmacists to optimise patients' pharmacotherapy in a community pharmacy setting using a collaborative care approach. The study was carried out on a sample of 80 patients in a community pharmacy setting. Two inclusion criteria were identified: patients ≥65 years and taking ≥3 medications. Patients were selected by convenience sampling from one community pharmacy. The GheOP³S[1] tool was applied to identify pharmaceutical care issues which were assessed by the researcher to identify necessary interventions. A tool was developed for the documentation of the pharmacist interventions. Pharmacist sessions were carried out either face-to-face or through telephone and patients were followed up after 2 months. A sample of three case studies having the most frequent pharmacist interventions were selected for validation of pharmacist intervention by an expert group, consisting of 3 community pharmacists and 3 general practitioners. A high level of agreement with the pharmacist interventions was demonstrated by the expert panel, validating the pharmacist interventions from a clinical relevance perspective. The mean number of medications the patients were taking was 7 (range 3-16). The mean interview time was 11 minutes for face-to-face interviews and 12 minutes for telephone interviews. Through the GheOP³S tool, the pharmacist identified 254 pharmaceutical care issues: 61% of the care issues concerned general care-related items, 13% related to potential prescribing omissions and 10% were associated with drug-drug interactions. The pharmacist carried out 190 interventions: 41% of the interventions dealt with checking the medication adherence of patients, 13% concerned patient education about a specific condition or medication and 12% were specific to influenza vaccine

recommendations. The pharmacist interventions were fulfilled with a 79% implementation rate. The study confirmed that remote clinical pharmacy services in primary care were effective at identifying care issues and implementing relevant pharmacist recommendations. The application of the GheOP³S tool in conjunction with the developed data collection tool was feasible and applicable in the community pharmacy context. The tools identified pertinent care issues and facilitated a standardised pharmacist intervention. The developed data collection tool ensures appropriate documentation and follow-up of the proposed interventions.

Reference:

1. Tommelein E, Petrovic M, Somers A, Mehuys E, van der Cammen T, Boussery K. Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S) tool. J Public Health (Oxf). 2016;38(2):e158-70.

Keywords: older patients; medication optimisation; explicit criteria; GheOP³S tool

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

COVID-19 – Coronavirus disease-2019

DOAC – Direct oral anticoagulant

DRP – Drug-related problem

FRAX® – Fracture risk assessment tool

GheOP^{3}S – Ghent Older People's Prescriptions community Pharmacy Screening

GP – General practitioner

MAT – Medication assessment tool

NICE – National Institute for Health and Care Excellence

NSAID – Non-steroidal anti-inflammatory drug

OTC – Over-the-counter

PCNE – Pharmaceutical Care Network Europe

PIM – Potentially inappropriate medication

PIP – Potentially inappropriate prescribing

POYC – Pharmacy of your choice

PPI – Proton pump inhibitor

PPO – Potential prescribing omission

RAAS – Renin–angiotensin–aldosterone system

SPSS – Statistical Package for Social Sciences

START – Screening tool to alert to right treatment

STOPP – Screening tool of older people's prescriptions

SWOT – Strengths, weaknesses, opportunities, threats

TMP/SMX – Trimethoprim/sulfamethoxazole

VKA – Vitamin K antagonists

Chapter 1

Introduction

1. Introduction

The contribution of the pharmacist in the optimisation of medication in the older population has been long demonstrated in various clinical settings (Lim et al., 2004; Browne et al., 2014; Andreassen et al., 2016; Chiu et al., 2018). Medicines optimisation may be directed to a specific condition or involve a more holistic approach, considering all the medications that a patient may be taking (Lee et al., 2015).

In the United Kingdom, a guide issued by the Royal Pharmaceutical Society (2013) discusses four key principles that need to be in place for medication optimisation to be carried out. These being: understanding the patient's situation, choosing evidence-based medicine, making medicine optimisation part of routine and ensuring safest medicine use. The ultimate aim is to improve patient outcomes. In the United States of America, the University of North Carolina's Center for Medication Optimisation through Practice and Policy outlines medication optimisation as "a patient-centred, collaborative approach to managing medication therapy that is applied consistently and holistically across care settings to improve patient care and reduce overall health care costs" (Easter and DeWalt, 2017; Farley et al., 2017). In the latter definition the notions of value-based care and a team-based approach are more apparent. It encourages interdisciplinary collaboration and holistic medication optimisation with the scope of improving patient outcomes and reducing healthcare costs. Both definitions have a patient-centred approach as the central idea in common.

Medication optimisation goes hand-in-hand with reducing potentially inappropriate prescribing (PIP). PIP can take several forms mainly being underprescribing, overprescribing or misprescribing (Spinewine et al., 2007). The pharmacist in the

community is proven to have a critical role in assessing medication appropriateness, particularly with the older population (Jokanovic et al., 2017). The latter paper identified literature sources which illustrate different types of medication reviews that can be carried out either by a community pharmacist or by a multidisciplinary team including a pharmacist.

1.1 Medication reviews

For several years the pharmaceutical community strived to define medication review to reconcile, as much as possible, the diverse cultural differences and patient settings. The Task Force on Medicines Partnership and The National Collaborative Medicines Management Services Programme suggested that a medication review should be defined as a structured analysis of a patient's treatment (Shaw et al., 2002). The review should be aimed at attaining a consensus with the patient about the treatment, optimising the impact of medicines, reducing the number of drug-related problems (DRPs) and curtailing waste. This definition was found not be comprehensive enough to include all countries internationally (Griese-Mammen et al., 2018).

The Pharmaceutical Care Network Europe (PCNE) sought to achieve a more internationally recognised definition of medication review. The organisation defined the term as being "a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting DRPs and recommending interventions" (Griese-Mammen et al., 2018). The publication recognises four different types of medication reviews, according to the information available to the healthcare professional, as illustrated in Table 1.1.

Table 1.1: Classification of the different types of medication reviews according to the PCNE

Type of medication review		Type 1	Type 2a	Type 2b	Type 3
Accessible information	Medication history	✓	✓	✓	✓
	Patient interview		✓		✓
	Clinical data			✓	✓
Icons used in the paper					

Adapted from Griese-Mammen et al., 2018

For the purpose of this study, the PCNE's definition was adopted as it provides a consensually agreed upon definition which is clearer at providing a structured comprehensive understanding of the term. By logic, it encompasses the essence of the first definition by Shaw et al. (2002).

There are a number of outcome measures which emanate from different types of medication reviews. Though medication reviews that focus more on medication adherence and quality of life result in outcomes that may be considered as 'humanistic', other reviews target more 'clinical' outcomes like blood pressure or cholesterol control. The overall goal of every medication review is to optimise a patient's treatment. Various studies demonstrate that medication reviews yield better disease management of older patients (Milos et al., 2013; Jokanovic et al., 2017; Lenander et al., 2018; Houlind et al., 2020).

Medication reviews can take place in all healthcare settings by either a pharmacist or a doctor on their own or by a multidisciplinary team (Blenkinsopp et al., 2012). While medication reviews are thought of being an important tool to improve healthcare outcomes, a recent meta-analysis by Huiskes et al. (2017) shows that when medication reviews are carried out as a short-term intervention irrespective of setting and patient characteristics, although drug-related outcomes may be improved, the same cannot be said for clinical and quality of life outcomes. One has to be specific in which instances it is most pertinent to carry out medication reviews. The authors argue that for example while age and number of drugs that a patient is taking are often used as inclusion criteria in studies, co-morbidity may be a more important characteristic to take into account (Huiskes et al., 2017).

Medication reviews with patient follow-ups in the community pharmacy, targeted to optimise drug treatment in older patients and to avoid medication-related problems, were shown to be significantly cost-effective (Malet-Larrea et al., 2017). To ensure effectiveness and efficiency, there are different factors that need to be in place for a community pharmacist to be able to undertake a comprehensive medication review. Workplace changes, practice support and education all have contributed to implement pharmacists' involvement in adequate pharmacotherapy management and treatment optimisation (Brandt et al., 2020).

1.2 Pharmacist-led interventions in the community setting

The term 'pharmacist-led intervention' is a broad concept whereby the pharmacist optimises patient's treatment in several health conditions or in a holistic way to the older population. Community pharmacist-led interventions have led to an improvement in adherence and health outcomes (Milosavljevic et al., 2018). The pharmacist's input in the area of geriatrics has been proven to be relevant in both inpatient and outpatient settings (Riordan et al., 2016; Chiu et al., 2018). Pharmacists have been shown to be key players in leading pharmaceutical care for the patients' benefit. Interventions vary according to the endpoint that is desired. Interventions that were shown to be effective for ambulatory older patients to improve medication adherence and health outcomes are multi-factorial and must be tailored to the patient's needs. Interventions may consist of an amalgamation of components comprising of patient education, monitoring and follow-ups (Marcum et al., 2017; Milosavljevic et al., 2018).

A specific study (Martin et al., 2018) proved that pharmacist-led interventions on older patients in the community setting led to medication optimisation. This randomised control trial carried out in Canada is very relevant to the area of interest in this research investigation as pharmacists used educational materials leading to a significant reduction in inappropriate prescribing (identified through 4 of the Beers criteria) amongst older patients. In the same trial, pharmacists intervened with both patients and their prescribers over a period of 6 months during which they assessed the results of the intervention. A significant finding in the study was that a considerable amount of patients (53%) taking sedative-hypnotics started the tapering process due to this intervention, with the vast majority eventually discontinuing their medication (Martin et al., 2018).

One particular study chose to illustrate a more specific dimension for the use of pharmacist-led interventions, as they evaluated patients' medications with the aim of improving patients' cardiovascular risks (Tsuyuki et al., 2016). The mean age of the sample studied fell into a slightly lower age category (mean age = 62 years). The learning point from this study is still applicable to the research area - that of community pharmacists intervening to bring about significant treatment optimisation. In this randomised control trial carried out in Canada, it was found that pharmacist interventions significantly lowered the risk of cardiovascular events. This was carried out through thorough patient assessments, suggesting treatment adjustments, communication with the patient's general practitioner (GP) and periodic follow-ups aimed to minimise several risk factors such as lipid profile, blood pressure and glycaemic control (Tsuyuki et al., 2016).

Research demonstrated that a community pharmacist's intervention in a sample of adults taking warfarin, with a mean age of 70.5 years (indicating an old cohort of patients), brought about treatment optimisation (Mifsud et al., 2019). This was accomplished by firstly undertaking a medication reconciliation in order to: detect DRPs, develop individualised treatment plans and recommend actions to optimise treatment and ultimately follow-up patients after two months.

1.3 Medication assessment tools

Medication assessment tools (MATs) are developed to aid in the evaluation of medication appropriateness. Such tools can be either implicit, explicit or a combination of both and all of which having their own advantages and disadvantages (Shelton et al., 2000). Explicit criteria are preferred when one wants objective evidence developed from

expert opinion whilst implicit criteria, albeit not being always reproducible, may be more holistic in nature (Spinewine et al., 2007; Dimitrow et al., 2011).

The use of MATs by clinical pharmacists, within a multidisciplinary team, have proven to be effective in optimisation of treatment in older adults in specific disease conditions such as stroke and atrial fibrillation. MAT application identified lacunae in clinical performance which were targeted to optimise patients' pharmacotherapy (Gauci et al., 2017; Gauci et al., 2019).

In her paper Reeve (2020), has outlined several tools that may be used for deprescribing in older patients. The author discusses the different tools available that can be used in general for the older persons for example the Beers criteria (2019 American Geriatrics Society Beers Criteria® Update Expert Panel, 2019) and the Medication Appropriateness Index (Hanlon and Schmader, 2013). Additionally it mentions tools to be used in specific disease states such as cancer like the OncPal Deprescibing Guideline (Lindsay et al., 2015). Having such tools available equips healthcare professionals in providing the most appropriate treatment to a range of diverse patients in different situations.

1.3.1 Explicit tools for optimising treatment in the older population

Explicit criteria aim to identify pharmaceutical care issues and then the pharmacist can intervene to bring about treatment optimisation. Several explicit tools have been identified in literature (Nicieza García et al., 2016) that can be adopted by pharmacists when undertaking medication reviews to assess medication appropriateness of older people in ambulatory care. These include the Beers Criteria

(2019 American Geriatrics Society Beers Criteria® Update Expert Panel, 2019) and Screening Tool of Older People's Prescriptions and Screening Tool to Alert to Right Treatment (STOPP/START) criteria (O'Mahony et al., 2015).

The Beers criteria is a set of criteria developed to optimise older patients' treatments updated periodically according to emerging evidence. The first edition targeted patients in nursing homes and later broadened to include all patient settings. It includes a set of drugs that should be avoided, those to be used with caution, drug-drug interactions that should be avoided, drug-disease interactions that may aggravate an illness and a list of drugs that should be avoided in renal function decline for the geriatric population (2019 American Geriatrics Society Beers Criteria® Update Expert Panel, 2019).

The STOPP criteria focus on potentially inappropriate medications (PIMs) while the START criteria identify potential prescribing omissions (PPOs). The purpose of these criteria is to optimise treatment for the older persons and prevent adverse drug reactions and adverse drug events. The STOPP/START criteria (which are European in nature) are categorised according to physiological systems and have been applied to a multitude of settings as an intervention, and yielded positive outcomes (O'Mahony et al., 2015). The STOPP criteria was found to be particularly applicable in a Maltese long-term elderly care setting to detect PIMs (Fenech Caruana, 2018).

The STOPPFrail criteria (Curtin et al., 2020) have been developed with the aim of guiding clinicians in assessing which older patients would benefit from deprescribing certain medications as they reach end of life. In this trial it was found that polypharmacy and medication costs are reduced with such a medication review. The same could not

be said for secondary outcomes like falls, quality of life and mortality where no substantial changes were registered during the period of investigation. The authors attributed this due to the fact that the study might have been underpowered.

Protocols evaluating patients' treatment more specifically within a community pharmacy setting remain sparse. The Ghent Older People's Prescriptions community Pharmacy Screening (GheOP^{3}S) tool is an example of an effective innovative tool which is adapted to the European scenario (Tommelein et al., 2016). Compared to the other previously mentioned tools, the GheOP^{3}S tool is more focused on carrying out a medication review for older patients living in the community. This contrasts substantially with the Beers criteria and STOPP/START tool which are less specific in their application in different patient settings and not targeted for a community pharmacy setup, as in the case of this research investigation.

1.3.2 The GheOP^{3}S tool

The GheOP^{3}S tool is an explicit set of eighty-three criteria that aims to identify PIP using the data which a community pharmacist has available. In the occurrence of PIMs, alternatives or safer approaches are recommended. A two-round Delphi technique was used to identify the criteria in the tool but this was further refined to exclude items that were although clinically relevant, were unfeasible in the community pharmacy setting. These mainly included criteria which made reference to renal impairment. This is understandable since community pharmacists do not have sufficient clinical data in this regard. The authors claim that further training is essential for the correct application and interpretation of the GheOP^{3}S tool (Tommelein et al., 2016).

This tool was validated by community pharmacists in Belgium and direct applicability to the Maltese scenario requires further psychometric testing. In Belgium, community pharmacists have access to dispensing data of both non-prescription and prescription medicines whilst this is not the case for Malta. Maltese community pharmacists only have access to the patients' chronic medication being dispensed free of charge via the Pharmacy of Your Choice (POYC) scheme, for the patients registered with their pharmacy.

Foubert et al. (2020) tested the GheOP^{3}S tool on a sample of community-dwelling older patients and revealed a number of DRPs. In the Foubert study, pharmacists made recommendations to GPs and most of the recommendations were accepted and implemented at 3-month follow-up. The authors observed that certain proposals like therapy monitoring were more accepted when compared to other recommendations like stopping treatment. Foubert et al. recommend that there should be a priority in the clinical actions that need to take place rather than implementing all actions at the same time.

Al Wazzan et al. (2018) developed an addendum to the GheOP^{3}S tool whereby a set of criteria have been established on "PIP of renally excreted active drugs" in geriatric polypharmacy patients. For such an evaluation to be possible, community pharmacists had to have the serum creatinine level at hospital discharge available. This addendum was applied to a sample of 60 patients but the authors state that the use of such serum creatinine level may not always be the patient's true value at the time of evaluation for PIP at the community pharmacy. Hence this was considered to be a limitation of the study.

In a study carried out in Serbia (Stojanović et al., 2020) both the GheOP^{3}S tool and the STOPP/START criteria were applied to a cohort of 422 patients attending a Gerontology Centre. The aim of the study was to compare the effectiveness of the two tools. Results led to the notion that the GheOP^{3}S tool was able to detect more PIP than the STOPP criteria whilst the START criteria detected PPOs more than the GheOP^{3}S tool.

The GheOP^{3}S tool is specifically designed to be applied to community-dwelling older patients. Its absence for the need of clinical laboratory values which are not normally accessible to the Maltese community pharmacist and the fact that it is widely cited in literature made it an optimal set of explicit criteria which can be used as a means towards achieving medication optimisation.

There is a move for explicit criteria to be integrated in automated systems for screening. The application of such criteria needs to be followed up with an evaluation of the overall holistic benefit to the patient by a healthcare professional (O'Mahony et al., 2015; Tommelein et al., 2016; 2019 American Geriatrics Society Beers Criteria® Update Expert Panel, 2019; Kympers et al., 2019).

1.4 The COVID-19 pandemic

This research dissertation was undertaken in the context of the unprecedented times of a pandemic. Worldwide health systems struggled to maintain the burden of both the widespread Coronavirus Disease 2019 (COVID-19) and to sustain the burden of other non-COVID-19 diseases. This was particularly relevant in this community-based study where certain medical follow-ups were relegated to secondary importance and therefore postponed. Some argued on the risk versus benefit of older people leaving their homes

and coming into contact with high risk people such as healthcare professionals and risk contracting the infection (Kretchy et al., 2021). This positioned the community pharmacist to play an integral role at primary healthcare to offer adequate follow-ups and provide information to patients.

The pharmacy community had a number of challenges to take care of in the developing situation. Pharmacists had to monitor and solve drug shortages and draft professional advice amongst other tasks. The COVID-19 pandemic led to spearheading the idea of digitalized pharmaceutical care. Pharmacists and healthcare professionals across the board turned to telephone meetings for consultations and patient education. They worked hard to keep on helping the vulnerable people such as the old or pregnant people but with minimal face-to-face contact to slow disease spread. The impact of these new processes remain yet to be evaluated (Liu et al., 2020). In this context, the research explored the feasibility of remote pharmacist-led patient medication review and follow-up.

1.5 Aims and objectives

The aim of this research was to assess the feasibility and applicability of clinical tools and to optimise patients' pharmacotherapy in a community pharmacy setting using a collaborative care approach. In order to address this aim the following objectives were identified:

- to apply an explicit tool to identify pharmaceutical care issues
- to develop a community pharmacist data collection tool
- to evaluate application of explicit criteria and documentation tools in a community pharmacy setting.

Chapter 2

Methodology

2. Methodology

This chapter comprises a description of the study setting, rationale for the choice of explicit criteria, development of the community pharmacist data collection tool, procedure followed for data collection, data handling and statistical analysis. The research tools used to collect data, namely the GheOP^{3}S tool and the developed community pharmacist data collection tool, are described. The majority of the data collected was categorical in nature and included some qualitative data collection.

2.1 The setting

The setting for this research is a community pharmacy in the south of Malta. The pharmacy is open from Monday to Friday from 7.30 am till 9.00 pm and Saturday from 7.30 am till 7.00 pm, excluding public holidays. On Sundays and public holidays, the pharmacy opens according the roster issued by the Malta Medicines Authority. The pharmacy represents a typical community pharmacy providing services to a good proportion of older persons living in ambulatory care.

In Malta a community pharmacy dispenses medications on the private market, which may consist of medications for either acute or chronic conditions. The pharmacy is part of the 'POYC' scheme which supplies chronic medication free of charge to patients depending on the patients' entitlements every eight weeks. The list of medications and pharmaceutical products that are given by the government is updated periodically by the Directorate for Pharmaceutical Affairs. Patients' entitlements vary according to whether they are in possession of a pink form or yellow card. The pink form is subject to means testing whilst the yellow card, known as the Schedule V, applies for patients suffering

from chronic diseases. Such schemes apply to all Maltese citizens, EU citizens living in Malta permanently, foreigners married to Maltese citizens, foreigners working and paying social contribution in Malta or receiving a Maltese state pension. Some drugs require special permits which need to be applied for by a specialist to be given free of charge.

An electronic system is available for all pharmacies participating in the POYC scheme. The identity card number and date of birth of the patient enables the pharmacist to access the patient's entitlement and a history of last dispensed medications. No patient laboratory results or discharge letters are to-date accessible to the community pharmacist. The supply of medicinal products is delivered to each pharmacy every week directly from the POYC unit as a replenishment of the drugs dispensed in the previous week. Any drug which is not available at the time when the patient presents to the pharmacy can be ordered urgently and a courier service delivers the medicine as necessary.

Official statistics show that in year 2017, 180,000 Maltese or Gozitan patients were availing themselves of this national free medicines scheme[1]. National statistical records indicate that 3.28 million pharmaceutical preparations dispensed in the Maltese islands, in the following year, were through the POYC scheme[2]. There is a well-known positive correlation that the older patients get, the greater the number of chronic conditions

[1] Ministry for Health. National outpatients' services' booklet. Valletta: Pharmacy of Your Choice Unit; 2017.

[2] National Statistics Office - Malta. Health Care Statistics 2018 [Internet]. Valletta: National Statistics Office - Malta; 2018 [cited 2021 May 4]. Available from: https://nso.gov.mt/en/publicatons/Publications_by_Unit/Documents/A2_Public_Finance/2020/info-health%20statistics%202018.pdf

patients suffer from and therefore the more chronic medications older patients are prescribed (Molokhia and Majeed, 2017; Pereira et al., 2017). By inference one can say that the majority of patients making use of the POYC service are predominantly old patients.

To start receiving their free medications, patients can choose the pharmacy they want to register with. The concept of registration with a particular pharmacy enables a rapport to be established with the patient's community pharmacist such that a more personalised pharmaceutical service can be delivered.

Up till the onset of the COVID-19 pandemic, prescriptions were needed each time the patients required a refill of their medications. At the present time, prescriptions are no longer required and the patients are advised to conduct regular check-ups with their GP and/or specialist and confirm or revise their prescriptions accordingly. There is no formal record of this procedure and so the pharmacist has a key role to ensure that patients are keeping their follow-up appointments. In Malta, medication reviews are not typically carried out formally by community pharmacists and there is no system in place which gives community pharmacists an incentive to carry out this task.

The day-to-day running of the POYC system generally follows a defined course of action. The patients, registered with the pharmacy, are given a date by which they have to inform the pharmacy either by telephone or in-person that they are due for their medication supply. The pharmacist then prepares their treatment and the patients come to the pharmacy to collect it. Another due date is given for their next supply. Each patient needs to inform his/her pharmacy whenever there is a change in treatment or

change in dosage regimen, via the presentation of a prescription to receive the required medication supply. At this point, the pharmacist is obliged to provide professional advice on the proper use of medication/s and any relevant support to the patient concerned.

A community pharmacy in Malta is manned by a minimum of one pharmacist and often aided by at least one sales assistant. Pharmacies usually stock a variety of products such as vitamins, dermo-cosmetics, baby products, perfumes, beauty products and other toiletries, besides medications. A GP is usually in attendance on a daily basis and specialists, or other healthcare professionals, on a fortnight or a weekly basis. The presence of the GP in the pharmacy facilitates both the accessibility for a medical opinion and the establishment of a vital professional relationship, between doctors and the pharmacist/s, which can aid decision-making on pharmaceutical care for the patient. GP services in Malta can be accessed through the national health service via regional health centres or privately.

2.2 Conceptual map

The following is a conceptual showing the logical steps involved leading to the development of the data collection tool used in this research. The starting point was the identification of the explicit criteria from various sources of literature. Then the data collection tool themes were drafted based on the recommendations of one of the most relevant set of explicit criteria which was recognized to be the GheOP^{3}S tool. This was followed by validity and reliability testing. The last step consisted of a number of trials as part of the pilot study. The entire process was visualized as occurring in a number of stages in the form of a 'funnel' approach as illustrated in figure 2.1.

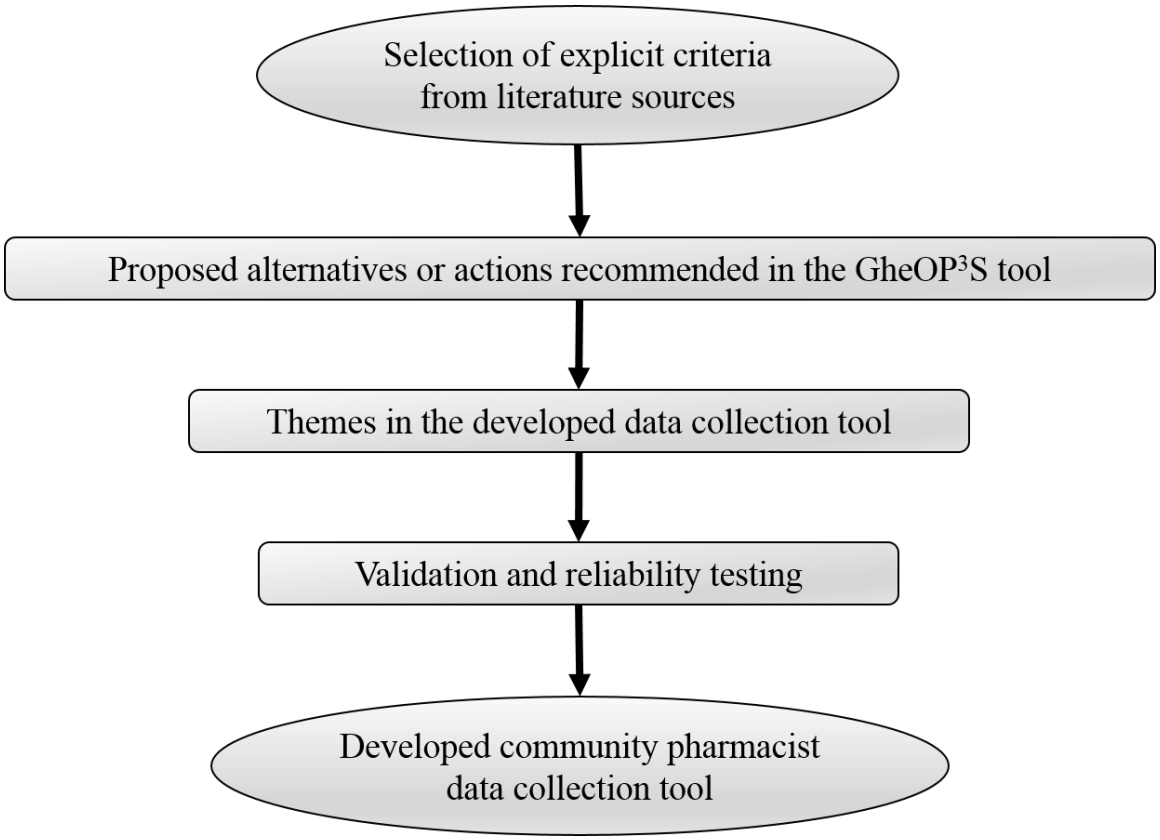


Figure 2.1: Approach to group the themes in the data collection tool

2.3 Selection of explicit tool

A thorough systematic literature search on the subject was conducted using articles from peer-reviewed journals. Articles were identified through online databases such as Google Scholar, PubMed and the University of Malta's database – 'HyDi'. This started in the preliminary phases and was kept ongoing throughout during the course of the entire research. The literature review that was carried out over a period of two years covered a number of relevant research areas such as the use of explicit criteria for optimisation of treatment in the older population in different health systems in other countries.

A Strengths, Weaknesses, Opportunities, Threats (SWOT) analysis was carried out to identify which explicit criteria, available from literature, were most apt to answer the research question. The GheOP^{3}S tool (Tommelein et al., 2016) was deemed most appropriate for the study since it is the only tool identified focusing on medication optimisation for older patients living in the community and developed within a European setting.

The criteria in the GheOP^{3}S tool are categorised in the following five sections (Appendix 4A):

- "Part 1a: Potentially inappropriate drugs, independent of diagnosis – drug classes"
- "Part 1b: Potentially inappropriate drugs, independent of diagnosis – specific molecules"
- "Part 2a: Potentially inappropriate drugs, dependent on diagnosis – drug classes"
- "Part 2b: Potentially inappropriate drugs, dependent on diagnosis – specific molecules"
- "Part 3: PPOs"
- "Part 4: Drug-drug interactions of specific relevance"
- "Part 5: General-care related items to be addressed in the community pharmacy" (Tommelein et al., 2016).

2.4 Developing the community pharmacist data collection tool

A separate body of literature that was reviewed related to pharmacist-led interventions in the community pharmacy setting. The development of an innovative standardised data collection tool was deemed necessary to measure the outcomes of the application of the GheOP^{3}S tool and to assess patient follow-ups, after two months.

2.4.1 Designing the research instrument

The data collection tool was developed such that record of the GheOP^{3}S interventions undertaken can be retained. The developed tool consists of three main sections.

i) The 'Patient profile' which includes the patient code number, number of medications, vitamins or supplements that the patient is taking, age, sex, list of chronic medications, list of chronic conditions, and whether the patient avails of a private or public GP service. In this section, the researcher has to specify whether the patient interview will be done face-to-face or via a telephone call.

ii) The 'Pharmaceutical care issues' section records the type of intervention carried out by the pharmacist (such as patient education or referral to a doctor) at time = 0, by means of ticking next to the appropriate intervention carried out. An alpha-numeric code was assigned for each pharmacist intervention. The number 1 was used for the pharmacist interventions carried out at baseline whilst number 2 was used for the follow-up phase. The 24 pharmacist possible pharmacist interventions at baseline were delineated (A1-X1), as presented in Appendix 1.

iii) The 'Effectiveness and sustainability of pharmacist intervention' part which enables documentation of the follow-up after two months, again by means of ticking - indicating the intervention was taken up. Another 24 possible follow-up actions (A2-X2) to the pharmaceutical care issues were delineated here, as shown in Appendix 1.

The two-month follow-up period was chosen to be in-line with the POYC timeline whereby patients collect their medication every eight weeks.

The duration of every patient interview was recorded to check for any difference between the time span of telephone and physical interviews. Recording the duration of the two instances, two months apart, would allow time duration analysis of the first-time interview and of the follow-up. The GheOP^{3}S tool throws light on the potential of a community pharmacist making an effective intervention, albeit the limitations regarding the ability of communicating with other healthcare professionals and the lack of laboratory results.

The developed data collection tool aims to evaluate the effectiveness of community pharmacists' intervention in optimising an older patient's chronic treatment through a collaborative care model. The final version used in the study can be found in Appendix 1. Changes in the current system for better patient follow-up from the community pharmacist's side were proposed.

2.4.1.1 Themes included in the data collection tool

The themes in the developed community pharmacist data collection tool were derived from the proposed alternatives or actions recommended in the GheOP^{3}S tool. The latter were grouped in a total of twenty-four themes as demonstrated in the following Table 2.1.

Table 2.1: Themes in the data collection tool

Theme code	Description of theme
A1	Referral to GP/specialist due to prolonged drug treatment
B1	Drug prescribed without an evidence-based indication
C1	Non-pharmacological approach should be considered
D1	Referral to GP/specialist depending on underlying condition
E1	Verification with GP/specialist should be undertaken
F1	Verification of whether a step-up approach was considered and adopted
G1	Referral to GP/specialist due to a safer alternative medication available
H1	Medication switch recommended by the pharmacist due to a safer alternative medication available
I1	Monitoring need
J1	Starting a drug at the lowest possible dose
K1	Referral to GP/specialist for dose reduction
L1	Referral to GP/specialist because the addition of another drug is needed
M1	The addition of another drug/vitamin is recommended by the pharmacist
N1	The omission of another drug/vitamin is recommended by the pharmacist
O1	Guidance on timing of medications/vitamins
P1	Patient education on a specific condition or medication
Q1	Discussion with GP/specialist needed
R1	Influenza vaccine recommendation
S1	Recommendation of assistance in medication or health issues (by nurse, neighbour, relatives etc.) in frail older patients or older patients with reduced cognition
T1	Discussion on aspects of pharmaceutical care that could be improved for the patient
U1	Verification or discussion on the patient's adherence to chronic medication
V1	Provision of a clear medication schedule to polypharmacy patients
W1	Verification that all over-the-counter (OTC) medication is listed on the patient's electronic record
X1	Any other pharmaceutical intervention not listed above

Ticking was used to show that the intervention was carried out. Each intervention that was ticked was then followed up in the same data collection tool with another tick if the intervention was maintained or recommendation taken up (Appendix 1).

2.4.1.2 Validity and reliability of the tool

The data collection tool was compiled and then validated by an expert panel consisting of three community pharmacists, two medical doctors and one layperson. This research instrument was validated for the syntax, data being sought and overall layout. The original plan was for the healthcare professionals to meet as a focus group to discuss the tool. Due to the COVID-19 pandemic restrictions the researcher had to opt for an alternative plan consisting in the remote collection of individual feedback from each healthcare professional.

Reliability testing for the data collection tool was carried out by two community pharmacists. Such an exercise was carried out to establish inter-rater reliability for the developed data collection tool, to ensure consistency in data collection. Fifteen older patients who were not included in the main study were chosen from a different community pharmacy so that the pool for the main study is not compromised. A case scenario for each of the 15 patients was recorded. The GheOP^{3}S issues flagged for each patient were prepared so that the developed data collection tool is the only variable, in order to test it out correctly. The researcher ticked which pharmacist interventions (from the data collection tool) would be recommended for each patient. Another community pharmacist went through each case and the relevant GheOP^{3}S issues. The same pharmacist then, similarly to the researcher, autonomously marked which interventions from the data collection tool she would lead herself where applicable. This was followed

by performing a statistical analysis using the Kappa test to ensure consistency in data collection.

2.4.2 Pilot study

A pilot study was carried out before the main study was initiated. This involved applying the GheOP^{3}S tool on five patients and recording the results on the developed community pharmacist data collection tool. This was done to test the feasibility of the study design and for the researcher to get used to the clinical tools that were going to be used in the main study. Minor changes were carried out in this phase namely clarification of text to avoid ambiguity in the language and to focus more on the data to be compiled.

2.5 Sampling

The GheOP^{3}S tool was applied to a targeted sample of 80 patients who are registered with one community pharmacy, identified by convenience sampling according to the relevant inclusion and exclusion criteria. Patients above 65 years of age on at least 3 regular medications, vitamins or supplements were included. It was felt that vitamins and supplements should be included as the GheOP^{3}S tool itself mentions the importance for older patients to be taking certain vitamins and supplements like calcium/vitamin D or folic acid. Patients were excluded from the study if they resided permanently in a nursing home, as this may have influenced the results in this community-based study, and if they had dementia which would have hindered quality data collection.

The patients were invited to participate in this study whilst they were collecting their POYC medications or buying chronic medications. Those who accepted were introduced to the researcher. An appointment was set-up for the first intervention to be

carried out in one of the clinics situated in the same pharmacy. When older patients chose not to visit the pharmacy (as per COVID-19 pandemic recommendations), but instead sent someone else to collect their medications on their behalf, the researcher explained the study to this third person. Additional clarification, on the purpose and procedure of the study, was given to some patients via a telephone call if there was the need. The researcher handed out the consent form and participant letter to these delegated persons. Such patients were eventually interviewed over the telephone, upon receipt of the signed consent form.

2.6 Ethics approval

Permissions were granted from the managing pharmacist of the pharmacy and the authors of the GheOP^{3}S tool, prior to conducting the main study. This was done in order to obtain authorisation to carry out the study and collect data for academic purposes. These were submitted to the University Research Ethics Committee and the approval was granted (Appendix 2).

2.7 Procedure

A medication history of each patient and identification of the possible pharmaceutical care issues flagged by the GheOP^{3}S tool was undertaken. This was carried out by reviewing the dispensing history from the POYC database, where applicable, prior to the encounter with the patient. When the patient did not avail him/herself of the POYC scheme, the researcher asked the patient for his/her medication history ahead of the meeting. A patient interview was carried out using the developed data collection tool.

The interview started off by first asking the patient some demographic data which included age, sex and whether they visit a private GP or health centre whenever he/she need medical assistance.

Figure 2.2 shows the main steps involved in data collection process which included the flagging of pharmaceutical care issues in line with the chosen GheOP^{3}S tool and the pharmacist-led interventions which were recorded in the data collection tool.

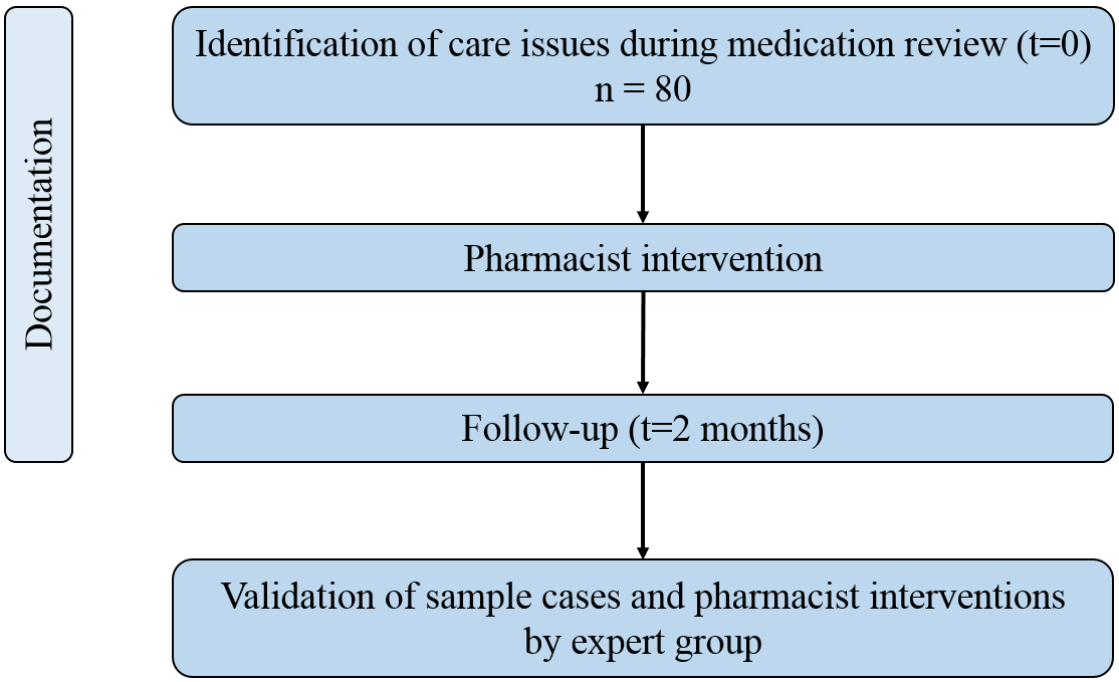


Figure 2.2: Flow chart showing steps of research design

The initial plan was to have face-to-face interviews but with the situation put forward by the COVID-19 pandemic, telepharmacy particularly for vulnerable patients including older persons had to be introduced. This reflected on the digitalised pharmaceutical care that was already available but which this pandemic has brought to the forefront. Patients who opted for telephone meetings had their follow-ups held over the telephone whilst those who were willing to have the meeting face-to-face were followed up in person, so

that continuity of the service could be maintained. Information from all interviews was recorded on the data collection tool. The data collection stage of the main study was carried out in the period between July and October 2020.

2.7.1 Identification of pharmaceutical care issues

The researcher took note of the patient's treatment in detail before the appointment taking place by making a list of the medications that were last dispensed to each patient according to the POYC's database available. The pharmacist created a password protected Microsoft® Excel sheet, for the patients who accepted to take part in the study and created a database including all drugs, vitamins and supplements which the patients get free of charge through the POYC scheme and those that they buy. In this way the number of medications that the patient is taking could be recorded. The treatment was verified with the patient him/herself for its completeness. Each patient was questioned about which chronic conditions he/she suffers from. Any potential pharmaceutical care issues were flagged on the GheOP^{3}S tool so that these were brought to discussion during the patient interview. Five out of the eighty-three criteria, in the GheOP^{3}S tool, were not relevant for the Maltese scenario as the drug mentioned was not available in Malta. These were "alizapride", "pentazocine", "ticlopidine", "alizapride with Parkinson's disease", "calcium and strontium ranelate".

It was noted that in the paper by Foubert et al. (2020) the GheOP^{3}S-criterion pertaining to rivaroxaban or apixaban being considered as PIMs (independent of diagnosis) was disregarded since recent evidence shows that the use of such drugs are generally preferred to warfarin in older patients (Pan et al., 2017; Sommerauer et al., 2017). DOACs have been promoted to first-line treatment in preventing stroke in patients with

atrial fibrillation in the NICE (National Institute for Health and Care Excellence) pathway (NICE, 2021). If the patient has a contraindication, does not tolerate or is not suitable to take a DOAC, warfarin should then be offered to the patient. It was decided that the presence of direct oral anticoagulants (DOACs) should be recorded for documentation purposes but should be disregarded as a pharmaceutical care issue.

2.7.2 Pharmacist intervention and follow-up

A medication review using the GheOP^{3}S tool was carried out, with a sample of eighty patients, using a combination of the medication information available to the pharmacist and the patient interview (but without clinical laboratory values or discharge case summary notes). Pharmacist intervention was provided according to the recommendations found in the GheOP^{3}S tool to bring about treatment optimisation, when necessary, and recorded in the developed community pharmacist data collection tool.

In accordance with the GheOP^{3}S tool, patients who were taking five medications or more were asked whether they would like a medication schedule in order for them to follow their treatment regimen in a more appropriate way. The template used by the researcher in this step was provided in two language versions (Appendix 3). The column headings were written in either English or Maltese to cater for the range in laypeople's knowledge according to the preferred language of the patient. A large font size and a clear font style were specifically chosen to help older patients in case of visual impairment. A revision date was included at the end so that the patient or healthcare professional making use of this document can confirm that this is most recent and updated version of the patient's treatment.

The patients were then followed up after a period of 2 months, following the pharmacist's intervention, so that the effectiveness and sustainability of the intervention could be determined. The time taken for the pharmacist to carry out both patient interviews was recorded. A time duration analysis for both patient interviews was carried out.

2.7.3 Clinical relevance of the pharmacist interventions

An expert group was consulted for validation of the pharmacist interventions carried out on the patients for clinical relevance. The group consisted of three community pharmacists and three GPs. These were invited to participate in a panel to evaluate the recommendations, indicating their agreement or otherwise with the interventions being proposed. A sample consisting of three patient cases was selected from the total of eighty patients recruited in the main study. These cases were carefully chosen on the basis of having a number of the most common pharmacist interventions proposed by the researcher.

2.8 Data handling

This section deals with the processing of raw data resulting from the following stages:

(i) reliability testing on the developed data collection tool

(ii) flagging of potential pharmaceutical care issues as highlighted by the GheOP^{3}S tool

(iii) processing of data from the data collection tool

(iv) recording of any improvement following the pharmacist intervention

(v) analysing the time duration for both interviews and

(vi) the clinical relevance exercise.

The primary outcomes in the study were the number and type of pharmaceutical care issues identified, the consequent pharmacist interventions, the implementation rate of these interventions and the time taken for the first medication review and respective follow-up to be carried out.

The results obtained in the reliability testing for the developed data collection tool were coded to enable quantitative analysis of data. This exercise analysed the inter-rater reliability of the data collection tool which had to be filled in with a tick – indicating a 'Yes' next to the appropriate pharmacist intervention which was deemed necessary. The IBM® Statistical Package for Social Sciences (SPSS) version 26[3] was used to analyse these data. The Kappa test was chosen to test reliability of these nominal scaled variables. The outcomes of this test indicate whether the data collection tool has inter-rater reliability at collecting the relevant data for the purpose of the study.

2.8.1 Data generated using the GheOP^3 tool

The pharmaceutical care issues that were flagged up while considering the GheOP^{3}S tool for each patient were recorded in Microsoft® Excel. This was categorised into the five sections in the GheOP^{3}S tool. For each care issue recorded a number 1 was marked in the appropriate box. The =COUNTIF function was used to get a count of the number of pharmaceutical care issues that were flagged out for each section of the GheOP^{3}S tool. Using these counts, one could calculate the percentage of care issues that were identified in each of the five sections in the GheOP^{3}S tool.

[3] IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.

2.8.2 Comparison of method of pharmacist consultation

Once the results were gathered using the data collection tool in the main study, one could determine the basic characteristics of the sample of older patients. A count and percentage of the type of pharmacist interventions carried out in the first encounter with the patient was generated. After the second encounter with the patients two months from the first interview, a count was kept as to how many of the pharmacist interventions were adopted by the patient and/or doctor as applicable. This was done to determine the percentage uptake of the pharmacist interventions by using the following formula:

$$\% \text{ uptake} = \frac{\text{number of pharmacist recommendations taken up}}{\text{pharmacist interventions proposed}} \times 100\ \%$$

In order to analyse whether there was any significant difference between the mean percentage implementation rates in both methods of consultations – face-to-face versus telephone, a statistical test was adopted. This consisted of a two sample proportion z-test which involved the use of an online Z-score calculator[4] to calculate the output for the data collected from the two interview methods employed in this research.

2.8.3 Time duration analysis

A paired samples t-test was carried out, using IBM® SPSS version 26, to see whether there was any statistical difference between the time taken to carry out the first medication review and the follow-up interview. This statistical test was chosen because the data is paired (for each patient there are two duration readings at t = 0 and t = 2).

[4] Social Sciences Statistics. Z Score Calculator for 2 Population Proportions [Internet]. Jeremy Stangroom; 2021 [cited 2021 Mar 20]. Available from: https://www.socscistatistics.com/tests/ztest/

An independent samples t-test was undertaken using the same computer program to determine whether there was any statistical significance between the mean interview times when patients were interviewed using the two different methods. This test was carried out twice – first to establish the presence or absence of any statistical difference between the mean duration at the initial interview and then again at the follow-up stage after two months.

2.8.4 Analysis of the clinical relevance exercise

The results obtained from the healthcare professionals who participated in the clinical relevance exercise were collated in a table for each of the 3 case studies. Separate percentage agreements were calculated between the three community pharmacists, the three GPs, and within the total group of six healthcare professionals in the expert group.

Chapter 3

Results

3. Results

This chapter analyses the data generated by applying the GheOP^{3}S tool, to a sample of older patients in a community pharmacy, and other data gathered from the newly developed data collection tool to record the pharmacist interventions carried out with these patients and during relevant follow-ups. The pharmaceutical care issues identified as well as the interventions performed, provided an insight on the key areas of how a community pharmacist can effectively improve pharmaceutical care for the geriatric population. An exercise taken up by an expert group aimed to show the clinical relevance, or otherwise, of the pharmacist interventions carried out throughout the period of this research investigation.

3.1 Validation of the developed data collection tool

Feedback from the community pharmacists, doctors and layperson was received regarding the layout and content of the tool. The GP trainee was of the opinion that the name of the patient's GP should be included in the patient profile for quick access and reference for the pharmacist, and this was included in the tool. One pharmacist recommended that vitamins and supplements like calcium should not be named specifically but rather grouped under the term 'vitamins'. A pharmacist and the GP trainee were sceptical on the phrase "Safer alternative medication available – medication switch by pharmacist". This was clarified by explaining the term 'medication switch' to apply exclusively for non-prescription drugs. The phrase in the data collection tool was applicable to situations such as switching the patient from ibuprofen to paracetamol.

One of the professional collaborators in this study suggested that "space intake of calcium from affected drugs" should be modified to "guidance on timing of medications"

since there might be other drugs apart from calcium which need spacing. The importance of including whether the patient can get medications free of charge to have better medication access was highlighted, especially since the study was targeting a pension-age section of the population. This concept was tackled within the data collection tool item T1 - "Aspects of pharmaceutical care that could be improved for the patient were discussed".

3.2 Reliability testing of the developed data collection tool

The results obtained during the inter-rater reliability testing of the developed instrument were analysed as highlighted in the methodology section 2.4.1.2. A Kappa test was run for each item included in the data collection tool and a p-value was obtained. For 11 items the Kappa value was 1 indicating perfect agreement between the two pharmacists. All the p-values for the remaining items, showed less than 0.05 level of significance. Hence, there was no significant variation between the two community pharmacists who decided about the pharmacist interventions needed, when consulting the GheOP^{3}S tool for a sample of 15 patients. The inter-rater reliability for all the data collection tool items used in this research was deemed satisfactory. The results of the inter-rater reliability assessment are represented in Table 3.1.

Table 3.1: Inter-rater reliability analysis of the agreement between the two pharmacists on the data collection tool items (A1-X1)

Item Code	Kappa value	Approximate T Value	p-value
A1	1.00	3.873	0.000
B1	1.00	Kappa not calculated due to perfect agreement	0.000
C1	0.595	2.519	0.012
D1 to H1	1.00	Kappa not calculated due to perfect agreement	0.000
I1	0.634	2.639	0.008
J1	1.00	Kappa not calculated due to perfect agreement	0.000
K1	0.634	2.639	0.008
L1 to O1	1.00	Kappa not calculated due to perfect agreement	0.000
P1	0.634	2.639	0.008
Q1	0.634	2.639	0.008
R1 to S1	1.00	Kappa not calculated due to perfect agreement	0.000
T1	0.444	2.070	0.038
U1	1.00	Kappa not calculated due to perfect agreement	0.000
V1	0.587	2.497	0.013
W1	0.444	2.070	0.038
X1	1.000	3.873	0.000

3.3 Pharmaceutical care issues identified using the GheOP^{3}S tool

This section deals with the demographic characteristics of the patients who participated in the study and the data gathered using the GheOP^{3}S tool, divided according to each of the five sections in the tool.

3.3.1 Demographic characteristics of participants

Out of a total of the 80 patients recruited in the study, 43 were female while 37 were male. The mean age of the patients was 70.9 years (ranging from 65-86 years). The mean number of chronic medications, supplements and vitamins that the patients were taking was 7 (ranging from 3-16 medications/vitamins). The majority of the patients (72) seek a private GP whenever they need to seek medical attention while 6 patients avail themselves of the free GP service available at the community health centre. Only 2 patients claimed that they never availed of any of the two options.

After consulting the patient's medication history and patient interview, 254 pharmaceutical care issues using the GheOP^{3}S tool were identified in this sample of 80 patients with a median of 3 (range 1-7) pharmaceutical care issues per patient. Three patients were lost to follow-up - one patient was undergoing chemotherapy while two patients lived far from the pharmacy and found it hard to attend the second consultation. Therefore 77 patients of the original sample were interviewed for a second time in the follow-up phase, after a period of two months.

3.3.2 Type of pharmaceutical care issues identified

Table 3.2 gives an account of the number of patients who were identified to have pharmaceutical care issues dealing with potentially inappropriate drug classes, independent of the patient's condition, using the GheOP^{3}S tool. The most prevalent pharmaceutical care issue from this category regarded the potentially inappropriate use of antidepressants for longer than a year, which effected 9 patients.

Table 3.2: Identified potentially inappropriate drug classes, using the GheOP^{3}S tool, independent of diagnosis

Item in the GheOP^{3}S tool		Number of patients	% of patients (n = 80)
1	Any antidepressant ≥ 1 year	9	11
2	Any antipsychotic drug ≥ 1 month	4	5
4	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥ 30 subsequent days	2	3
5	Any short- or long-acting benzodiazepine	2	3
8	Any oral non-steroidal anti-inflammatory drug (NSAID)	2	3
9	Any proton pump inhibitor (PPI) at full dose ≥ 8 weeks	2	3
11	Any sedating antihistaminic drug	2	3
Total number of care issues classified as "potentially inappropriate drug class, independent of diagnosis"		23	

Section 2b of GheOP^{3}S tool screens for potentially inappropriate drugs (specific molecules) independent of the diagnosis. These criteria identified only two care issues

at baseline: one patient who was on dipyridamole monotherapy and one patient on rivaroxaban. No other issues were identified following application of criteria from this section.

Table 3.3 shows the number of patients identified to have a pharmaceutical care issue dealing with potentially inappropriate drug classes dependent on diagnosis using the GheOP^{3}S tool. The most prevalent issue in this section was the use of a calcium channel blocker in patients suffering from constipation.

Table 3.3: Identified potentially inappropriate drug classes, using the GheOP^{3}S tool, dependent of diagnosis

Item in the GheOP^{3}S tool		Number of patients	% of patients (n = 80)
32	Any antipsychotic other than quetiapine and clozapine with Parkinson's disease	1	1
33	Anticholinergics with dementia or cognitive impairment	1	1
34	Anticholinergics with constipation	2	3
36	Calcium channel blockers with constipation	7	9
37	Non-selective β-blockers with asthma or chronic obstructive pulmonary disease	3	4
40	Thiazide and loop diuretics with gout	2	3
Total number of care issues classified as "potentially inappropriate drug class, depending on diagnosis"		16	

Considering potentially inappropriate drugs (specific molecules) dependent of diagnosis, as per section 2b of the GheOP^{3}S, no PIP was identified in the sample population studied. The criteria in this section relate to the use of alizapride or metoclopramide in patients diagnosed with Parkinson's disease.

With regards to PPOs, 28 patients were not reminded and recommended to undergo yearly influenza vaccination. Six patients (7.5%) had an elevated risk for osteoporosis (determined via the fracture risk assessment tool (FRAX®)) and were not prescribed calcium/vitamin D supplementation. Thus in total, a total of 34 patients were identified as have a PPO with application of the tool.

Table 3.4 shows the number of patients who had a drug-drug interaction of specific relevance, according to the GheOP^{3}S tool. The most commonly identified issue in this case was the concurrent use of cardioselective β-blockers with oral antidiabetic medications or insulin.

Table 3.4: Identified drug-drug interactions of specific relevance identified with the GheOP^{3}S tool

Item in the GheOP^{3}S tool		Number of patients	% of patients (n = 80)
50	Renin–angiotensin–aldosterone system (RAAS) inhibitor + potassium sparing diuretic/potassium supplements/potassium containing drugs	5	6
61	RAAS inhibitor + oral NSAID	1	1
64	Oral antidiabetics/insulin + non-selective β-blocker	4	5
65	Oral antidiabetics/insulin + cardioselective β-blocker	9	11
74	Calcium + levothyroxine	3	4
75	Bisphosphonate + calcium, magnesium, zinc, iron or aluminium	1	1
77	Any combination of anticholinergic drug	1	1
Total number of care issues classified as "Drug-drug interactions of specific relevance"		24	

Table 3.5 reveals the number of patients who had general care-related issues that could be addressed at the pharmacy. Adherence for chronic medications had to be checked in all patients as no records of checking adherence were in place.

Table 3.5: Summary of results obtained using the GheOP^{3}S tool for general care-related items to be addressed in the community pharmacy

Item in the GheOP^{3}S tool		Number of patients	% of patients (n = 80)
78	Dispensation of OTC medication was not added in the electronic patient record.	19	24
81	The patient was not asked which aspects of pharmaceutical care could be improved for him/her	4	5
82	Adherence for all chronic medication was not checked or discussed during the past year. Adherence for all new medication was not checked or discussed at first refill during the past year?	80	100
83	Polypharmacy patients (chronically taking five or more drugs) were not questioned about whether a clear medication schedule was available to him/her.	52	65
Total number of care issues classified as "general care-related items to be addressed in the community pharmacy"		155	

There were a number of GheOP^{3}S criteria which were not applicable for the cohort of patients under study (Appendix 4B).

Figure 3.1 shows the distribution of type of pharmaceutical care issues with the GheOP^{3}S tool, according to the classification in the tool itself. The largest proportion of the issues were related to general care-related items followed by PPOs. There were no patients who were taking a specific drug from a potentially inappropriate drug class when taking into consideration their diagnosis.

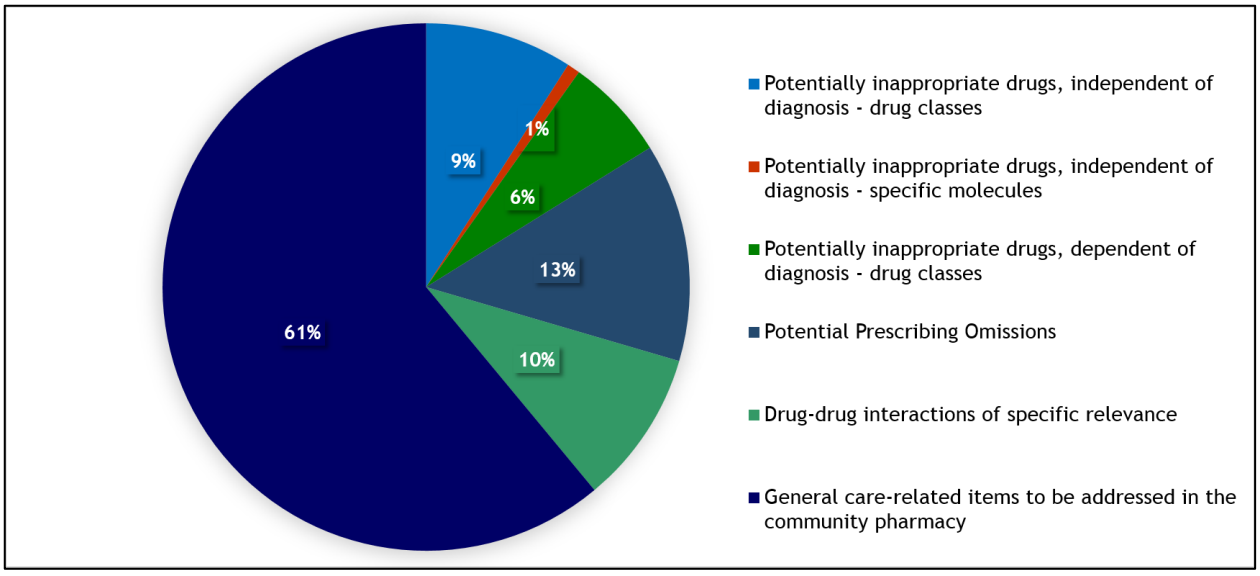


Figure 3.1: Pharmaceutical care issues identified

The five most prevalent pharmaceutical care issues detected were "adherence for all chronic medication was not checked or discussed during the past year" (80 patients), "polypharmacy patients were not questioned about whether a clear medication schedule was available to him/her" (52 patients), "the patient is not reminded and proposed to undergo yearly influenza vaccination" (28 patients), "dispensation of OTC medication was not added to the electronic patient record" (19 patients), "any antidepressant ≥ 1 year" (9 patients) and "oral antidiabetics/insulin + cardioselective β-blocker" (9 patients).

3.4 Pharmacist interventions

Upon patient interview, the pharmacist interventions were carried out depending on the pharmacist's clinical judgement. From the 254 pharmaceutical care issues identified, the pharmacist carried out 190 interventions. Figure 3.2 shows the most common pharmacist interventions carried out in a bid to improve the patients' treatments.

Checking the adherence for all chronic medication was the predominant intervention undertaken by the pharmacist. This was applied to all participants.

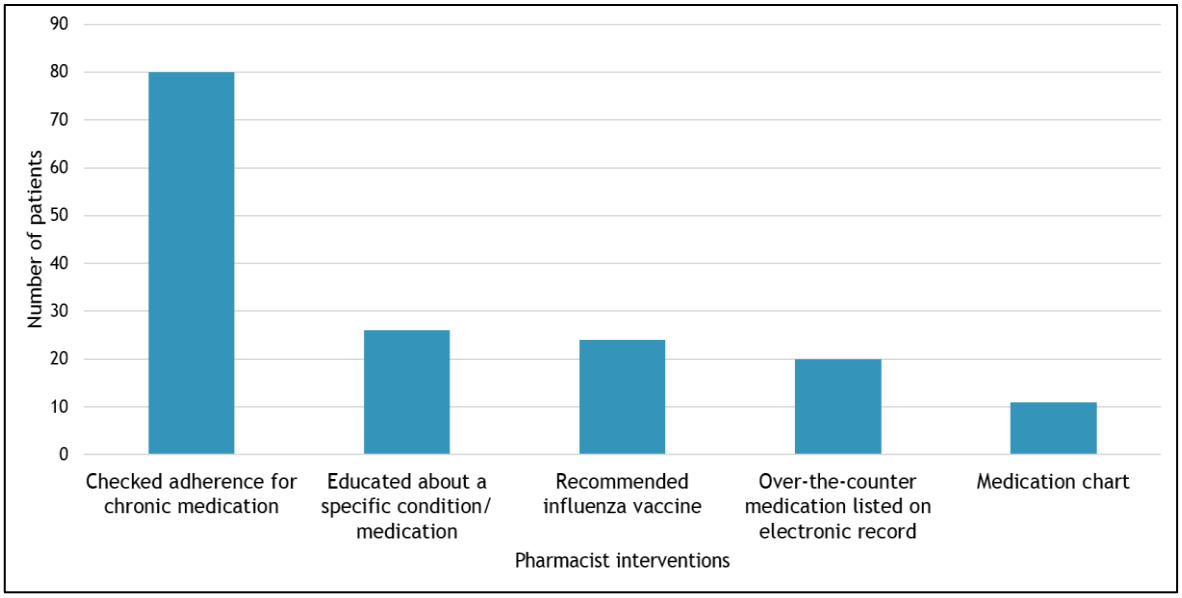


Figure 3.2: Interventions generated from identified care issues (t = 0)

3.4.1 Follow-up after 2 months

The percentage implementation rate of the pharmacist interventions were computed using the equation cited in section 2.8.2. In tables 3.6 and 3.7, the recommendations (at t = 0) for those three patients who withdrew from the study at the follow-up step were removed. This was done because one could not analyse the implementation rate for these recommendations without any follow-up investigation.

Table 3.6: Implementation rates of pharmacist interventions (part 1)

Pharmacist interventions	Rate of implementation (%) (implementations / recommendations)
Checking adherence to chronic medication & maintaining it	100 (77/77)
Patient taking a drug without an evidence-based indication and was referred to a doctor to stop treatment	100 (2/2)
Patient changing timing of medications/vitamins as advised by the pharmacist	100 (2/2)
Listing a patient's OTC medication on an electronic record	90 (19/21)
Maintaining patient education about a specific condition/medication	77 (17/22)
Patient monitoring following pharmacist's recommendation	75 (6/8)
Proposing change in pharmaceutical care plan was effective for the patient	75 (3/4)
Recommending and uptake of influenza vaccine	58 (14/24)
Providing and patient use of a clear medication schedule	56 (5/9)
Patient fixing an appointment with a doctor following pharmacist's referral for prolonged drug treatment	50 (3/6)
Patient satisfied with the safer alternative medication proposed by the pharmacist	50 (1/2)

Table 3.6: Implementation rates of pharmacist interventions (part 2)

Pharmacist interventions	Rate of implementation (%) (implementations / recommendations)
Recommending vitamin/medication by pharmacist and the patient followed the advice	20 (1/5)
Non-pharmacological approach proposed was effective in managing a condition	0 (0/2)
Dose reduction following recommended referral to doctor	0 (0/3)
Patient referred to a doctor for an underlying condition	0 (0/1)
Patient referred to a doctor because a safer alternative medication is available to be prescribed	0 (0/1)
Self-shielding of patient due to COVID-19 pandemic, with patient deprived access to doctors/specialist. Reassurance of pharmacist and GP assistance via telephone call was given. *It was highlighted that in life-threatening situations such as angina he should not fail to call for emergency.*	0 (0/1)
Recommended the free provision of blood glucose meter and use of lancing device to monitor blood glucose regularly	(*)
Total pharmacist interventions that were implemented	79 (151/190)

* This was the only recommendation that was given during the follow-up phase, rather than during the baseline meeting. Hence implementation rate does not apply here.

Table 3.6 shows that maximum implementation was achieved in pharmacist interventions pertaining to medication adherence, drugs without an evidence-based indication and timings of medications/vitamins. Appendix 5 shows which type of pharmacist interventions were carried out in the first interview and how many of them were taken up after a period of two months.

The results were analysed to see whether there was any difference between the implementation rate for face-to-face interviews versus telephone interviews and the findings were tabulated as follows.

Table 3.7: Mean number of pharmacist recommendations/implementations and implementation rates for face-to-face and telephone consultations

	Face-to-face (n = 50)	Telephone (n = 27)
t = 0 months		
Mean number of 'recommended' pharmacist interventions per patient (± standard deviation)	2 (± 1)	3 (± 2)
Total number of pharmacist recommendations = **R**	116	74
t = 2 months		
Mean number of 'implemented' pharmacist interventions per patient (± standard deviation)	2 ± 1	2 ± 1
Total number of implemented interventions = **I**	95	56
Implementation rate = $\frac{\mathbf{I}}{\mathbf{R}} \times \mathbf{100\%}$	82%	76%

The mean number of pharmacist interventions carried out in the first interview was higher in the case of telephone conversations while the average number of interventions was the same for both telephone and face-to-face follow-ups, at t = 2 months. The implementation rate for face-to-face interviews was found to be greater than that for telephone interviews.

There is a higher degree of variation in the number of pharmacist interventions carried out over the telephone at baseline. The standard deviation is the same for both types of interviews at the two-month follow-up stage. The z-test was used in order to determine whether the difference between the two mean implementation rates is statistically significant and the following results were obtained.

Table 3.8: Z-score measuring the difference in proportions for the two interview methods

	Face-to-face interventions	Telephone interventions
Recommendations	116	74
Implementations	95	56
z-score	1.0349	
p-value	0.2984	

From table 3.8 one can deduce that the difference between the two proportions (i.e. recommendation : implementation ratios) for the two methods of interview is not significant.

3.5 GP practice and uptake of pharmacist recommendations

Table 3.9 shows how the implementation rate of the pharmacist interventions varied when segregating the patients according to whether they have a private GP or attend the health centre. The sample is skewed towards having a private GP.

Table 3.9: Mean implementation rate of pharmacist interventions according to the patient's choice of GP

Patient's choice of GP	Mean implementation rate of pharmacist interventions (%)
Private GP (n = 69)	83
Health centre (n = 6)	94
Both private GP and health centre (n = 1)	100
Neither has a private GP and nor visits the health centre (n = 1)	50

3.6 Time taken for patient interview

Considering both face-to-face and telephone consultations, the mean time taken to undertake the first medication review was 11.3 minutes while the mean interview time for the follow-up was 2.8 minutes. Table 3.10 shows the paired sample t-test was carried out to analyse whether there is any significant difference between the mean duration of the first interview at t = 0 and the second one at t = 2 months.

Table 3.10: Comparing the mean interview times for the two paired samples at t = 0 and t = 2 months

	Mean	n	Standard deviation	Standard error mean
t = 0	11.34	77	7.55	0.86
t = 2	2.77	77	2.28	0.26

This table shows that there was a higher degree in time variation in the first interview as opposed to the second interview, which had a lower standard deviation. The positive correlation shown in table 3.11 indicates that the longer the interview time at t = 0, the longer the interview time was at t = 2 months.

Table 3.11: Paired samples correlations

	n	Correlation	Significance
t = 0 & t = 2	77	0.48	0.00

Table 3.12 gives the paired samples t-test carried out for the interview times for the consultations carried out at baseline and that after two months.

Table 3.12: Paired samples t-test for time duration in the two interviews

	Paired Differences					t	df	p-value (2-tailed)
	Mean difference	Standard deviation	Standard error mean	95% Confidence interval of the difference				
				Lower	Upper			
(t=0) – (t=2)	8.57	6.75	0.77	7.04	10.10	11.14	76	0.00

df = degrees of freedom

The p-value is less than 0.05 showing that there was a significant difference in the mean duration to carry out a medication review by the pharmacist between t=0 and t=2.

Table 3.13 demonstrates the mean interview times, along with the standard deviations, for both methods of medication reviews.

Table 3.13: Mean interview times for both modes of consultations

Mode of interview (n = 80)		Face-to-face		Telephone	
Mean interview time ± standard deviation	t = 0 months	11 ± 6 mins	n = 53	12 ± 9 mins	n = 27
	t = 2 months	3 ± 2 mins	n = 50	3 ± 2 mins	n = 27

Statistical analysis showed that in the first interview, telephone consultations tended to be slightly longer on average than the face-to-face interviews. Telephone medication reviews proved to have a considerably greater standard deviation corresponding to a greater time variation than those carried out in-person. The same could not be said after the subsequent follow-up after a period of two months, where the mean interview time

and standard deviation were identical for both types of interviews indicating consistency between the two modes of interview in all stages of the study.

An independent samples t-test was carried out to analyse whether there is any difference between the time taken for the medication review to be carried out face-to-face versus over the telephone at t = 0. Table 3.14 gives the group statistics for both categories of interviewees, i.e. the group which carried out the medication review in-person and the group which carried out the consultation over the telephone.

Table 3.14: Group statistics for both groups at t = 0

Group	n	Mean duration (minutes)	Standard deviation	Standard error mean
Face-to-face	53	11.22	6.48	0.89
Telephone	27	12.13	9.47	1.82

Table 3.15 gives the results of the independent samples t-test for the mean interview time at t = 0 for both groups.

Table 3.15: Independent samples t-test for time duration at t = 0

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	p-value	t	df	p-value (2-tailed)	Mean diff.	Standard error diff.	95% confidence interval of the difference	
									Lower	Upper
Time	Equal variances assumed	2.50	0.12	-0.50	78	0.62	-0.90	1.80	-4.48	2.68
	Equal variances not assumed			-0.45	38.78	0.66	-0.90	2.03	-5.00	3.20

df = degrees of freedom; diff. = difference

The Levene's test assesses whether the variances between the two groups are equal or not. The Levene's p-value (0.12) surpasses the 0.05 level of significance indicating that the two sample standard deviations do not vary significantly. When comparing the two mean scores using the Independent samples t-test the p-value is 0.62 indicating that the two mean scores do not differ significantly. There is no difference in the mean duration to carry out a medication review by a pharmacist when conducting it face-to-face versus over the telephone. These results prove that there is uniformity between the two methods of interview at baseline.

Another independent samples t-test was carried out to analyse whether there is any difference between the time taken for the medication review to be carried out face-to-face versus over-the-telephone reviews at the follow-up stage (t = 2 months). Table 3.16 gives the group statistics for the two categories of respondents, two months from the first interview.

Table 3.16: Group statistics for both groups at t = 2 months

	Group	n	Mean duration (minutes)	Standard deviation	Standard error mean
Time	Face-to-face	50	2.58	2.18	0.31
	Telephone	27	3.13	2.47	0.48

The independent samples t-test for the mean interview time in the follow-up phase is illustrated in table 3.17.

Table 3.17: Independent samples t-test for the mean interview time at t = 2 months

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	p-value	t	df	p-value (2-tailed)	Mean diff.	Standard error diff.	95% confidence interval of the difference	
									Lower	Upper
Time	Equal variances assumed	1.11	0.30	-1.01	75	0.32	-0.55	0.55	-1.64	0.54
	Equal variances not assumed			-0.97	47.89	0.34	-0.55	0.57	-1.69	0.59

df = degrees of freedom; diff. = difference

The Levene's p-value (0.30) once again exceeds the 0.05 level of significance indicating that the two sample standard deviations do not vary significantly. When comparing the two mean scores using the Independent samples t-test, the p-value was found to be 0.32 indicating that the two mean scores do not differ significantly.

There is no difference in the mean duration to carry out a medication review by a pharmacist when conducting it face-to-face versus over the telephone at t = 2 months either. Such results demonstrate that there is uniformity between the two methods of interview at the follow-up stage.

3.7 Validation of the pharmacist interventions for clinical relevance

An expert group, consisting of three community pharmacists and three GPs, was consulted to determine the level of agreement with the pharmacist's interventions. The following are the results obtained for the sample of three patient cases studies chosen, which are described in Appendix 6.

Table 3.18: Case 1 – agreement with the pharmacist's interventions

Intervention	Healthcare professional agreement (%)		
	Pharmacists n = 3	GPs n = 3	Total n = 6
1. Reduction in dose of benzodiazepine - referral to GP/specialist.	33.3	100	66.7
2. Patient education on sleep hygiene.	100	100	100
3. Patient education on anticholinergic side-effects due to a combination of anticholinergic drugs.	100	100	100
4. Influenza vaccine recommendation as the patient does not usually take it.	100	100	100
5. Adherence for all chronic medication was checked or discussed for the past year.	100	100	100
6. Provision of a clear medication schedule.	100	100	100
7. Patient did not have OTC medication listed on the patient's electronic record, so such medications were noted on an alternative electronic record available to the pharmacist for follow-up purposes.	100	100	100

From a total number of 42 evaluations by the six healthcare professionals on the 7 pharmacist interventions, 40 agreed with the intervention carried out. The expert panel was in concordance with the pharmacist interventions carried out except for the one pertaining to reduction in the dose of benzodiazepine which registered a disagreement between the pharmacists and the GPs.

Table 3.19: Case 2 – agreement with the pharmacist's interventions

Intervention	Healthcare professional agreement (%)		
	Pharmacists n = 3	GPs n = 3	Total n = 3
1. Monitoring need of blood glucose levels.	100	66.7	83.3
2. Patient education on the use of osmotic laxatives when the patient is constipated (may be linked to the use of amlodipine).	100	100	100
3. Patient education on possible changes in awareness of hypoglycaemia (metformin + atenolol may decrease hypoglycaemia awareness).	100	66.7	83.3
4. Influenza vaccine recommendation as the patient does not usually take it.	100	100	100
5. Adherence for all chronic medication was checked or discussed for the past year.	100	100	100
6. Patient did not have OTC medication listed on the patient's electronic record, so such medications were noted on an alternative electronic record available to the pharmacist for follow-up purposes.	100	100	100

There was again a noteworthy level of agreement among experts on the pharmacist interventions in the second case study. Out of a total of 36 evaluations, there was general consensus in 34 instances. In 4 of the interventions, all healthcare professionals agree completely with the type of interventions carried out by the pharmacist. Disagreement could be observed between pharmacists and GPs when evaluating interventions 1 and 3.

Table 3.20: Case 3 – agreement with the pharmacist's interventions

Intervention	Healthcare professional agreement (%)		
	Pharmacists n = 3	GPs n = 3	Total n = 3
1. Monitoring need of blood glucose levels.	100	66.7	83.3
2. Patient education on possible changes in awareness of hypoglycaemia (metformin + sotalol may decrease hypoglycaemia awareness).	100	100	100
3. Influenza vaccine recommendation as the patient does not usually take it.	100	100	100
4. Adherence for all chronic medication was checked or discussed for the past year.	100	100	100
5. Patient did not have OTC medication listed on the patient's electronic record, so such medications were noted on an alternative electronic record available to the pharmacist for follow-up purposes.	100	100	100
6. Aspects of pharmaceutical care that could be improved for the patient were discussed. It transpired that an updated prescription for an increase in daily dose of antidiabetic treatment was needed so her entitlement could be modified.	100	100	100

In the third case study, the expert panel confirmed the interventions in 35 out of 36 evaluations performed. In 5 of the interventions, the six healthcare professionals were concordant with the pharmacist on the interventions carried out. Pharmacists and GPs were discordant when evaluating the need to monitor blood glucose levels in the patient concerned.

3.8 General findings

The most significant findings for the quantitative data analysis in this study were the identification of pharmaceutical care issues in this patient cohort, the consequent pharmacist interventions and the validation of the pharmacist interventions by an interprofessional healthcare panel. The majority of the pharmaceutical care issues were "general care-related items to be addressed in the community pharmacy" with the need to check adherence to chronic medication found in all patients resulting in the most common pharmacist intervention being discussing adherence. More than half of the sample also required questioning about whether or not they have a clear medication chart available for their reference. The relevance of the pharmacist interventions was confirmed by majority consensus in the expert panel.

Chapter 4

Discussion

4. Discussion

This chapter discusses the main research outcomes of the study. It delves into the themes in which a community pharmacist, using the GheOP^{3}S tool, can intervene to bring about medication optimization to the older patient taking multiple medications. The chapter highlights the strengths and limitations of the study while providing recommendations for further research. It concludes with an overview of the research findings.

4.1 Evidence supporting medicines optimisation processes in older persons

Literature suggests that explicit tools help to detect inappropriate prescribing in the older population. Explicit criteria aim to identify pharmaceutical care issues to enhance pharmacist intervention and ensure optimisation of treatment. The GheOP^{3}S tool was identified and adopted in this study after researching peer-reviewed articles on medication reviews for older patients, in the community setting. The latter tool was found to be most effective to address the research question since it is specifically aimed at community pharmacists. It takes into account the reality that community pharmacists face, whereby they may have only limited clinical information available such as laboratory results to evaluate patients' treatment and outcomes. It is appropriate and applicable to the typical situation in Maltese community pharmacies, which lack accessibility to such useful resources.

Literature review considered other clinical tools applicable to older patients in all settings and are used to optimise treatment, such as the Beer's criteria and STOPP/START criteria. Other relevant areas of literature that were explored for this study included deprescribing and digitalised pharmaceutical care. The medication

review employed in the study is a 'type 2a' as described in the classification provided by the PCNE (2016). This factors in the patient's medication history and direct interaction of healthcare professionals with the same patient.

Maltese patients have the facility to access GPs either through public-run health centres or private health care services. In this study, the majority of patients were being followed-up by a private GP. This is reflective of the general Maltese trend whereby the majority of patients prefer attending their private GP whenever they need medical assistance, rather than visiting a health centre.

This research strongly demonstrated that there is a high implementation rate of the pharmacist interventions irrespective of the patient's choice of GP – whether private or public. Having a larger sample of patients who attend the health centre could have provided the researcher with more sufficient clinical data to compare any similarities and differences between the two different medical service providers. Whilst there is a great potential for community pharmacists to carry out medication reviews, there are still several challenges for Maltese community pharmacists to undertake such essential tasks aimed at customising and optimizing patient's treatment. These include: the lack of financial incentives to spend time carrying out medication reviews, the absence of a systematic structure or policy in place to carry out such reviews – both as an independent practitioner as well as within a collaborative practice with a GP service, weak communication between the community pharmacist and the GPs working at the health centre, the lack of clinical data and discharge letters available to the pharmacist and the difficulty in screening for high risk patients who would benefit mostly from the medication review as in the case of patient experiencing multimorbidity.

The GheOP^{3}S tool originated within the Belgian setting. One can compare the Belgian studies by Foubert et al. (2020) and Kympers et al. (2019) and this study due to extensive similarities in the methodology. In all three studies the GheOP^{3}S tool was used as a categorical screening tool by community pharmacists to detect PIP in a sample of older patients. The sample sizes were similar to each other and all assessed patients in primary care. In the Kympers et al. study, part 5 of the GheOP^{3}S tool, consisting of general pharmaceutical care-related items was not taken into account since it was carried out on a sample of patients that were recently admitted in a geriatric ward, rather than being present in a community setting. In the latter paper which addressed primary care treatment, the only patients considered for investigation were those who had not been hospitalised within the preceding 3 months. This measure was taken to eliminate any possible interference from any changes that could have been carried out in secondary care as these would have an impacted on the results of the main study.

In the Foubert et al. (2020) study, acceptance of the GheOP^{3}S issues flagged out relied on a face-to-face meeting between the pharmacist and GP succeeded by a follow-up episode after three months. In contrast, in the Kympers et al. (2019) study such a follow-up stage after the period of the implementation phase was not carried out. Nevertheless the hospital geriatrician's acceptance of the recommendations was considered before implementing any changes in the treatment plan. In this Maltese study, the patient was involved in relaying the proposed pharmacist intervention to the GP and the follow-up phase was carried out two months from the baseline intervention. This is realistic of the Maltese primary care setting where there are no structured interdisciplinary meetings held between healthcare professionals within the primary care setting.

4.2 Impact of pharmaceutical care issues identified

The most common pharmaceutical care issues noted in this research pertained to the "general care-related items to be addressed in the community pharmacy" section, of the GheOP^{3}S tool. In this section all patients had their adherence to chronic medication discussed, since the pharmacist had no record of the patients ever being probed about their adherence. In day-to-day practice, the pharmacist is not aware when the patients are due for their chronic medication refill and only checks when the patient claims that he/she is due for his/her medication (provided that the patient is registered with a particular pharmacy as part of the national free medication scheme – POYC scheme). Although the pharmacist has access to the patient's profile on the POYC database, the pharmacist can only check the dispensing history for medications being given through the POYC scheme and the refill rate.

The results pertaining to the medication adherence criterion could not be directly compared to the Foubert study (2020) as in the mentioned study the authors analysed nonadherence, whereas in the Maltese context the pharmacist does not have a measure available to assess such patient adherence. In this research patient adherence was checked through a verbal discussion between pharmacist and patient after two months and the participants were all found to be adherent to their pharmacotherapy. Adherence was particularly found to be the commonest GheOP^{3}S criterion detected in a recent study by Tommelein et al. (2017).

Within the setting of the study, the patient buys other acute or chronic medication, supplements or vitamins which are not supported through the POYC scheme. Given that local community pharmacists have no access to the dispensing history for such

medications, supplements or vitamins, it is an arduous task for pharmacists to keep track of the patient's level of adherence. When it comes to private market dispensing, the patient may be buying medications from multiple pharmacies. This makes it more challenging for a complete evaluation on the patent's overall adherence to his/her treatment and continues to highlight the importance of establishing a direct contact with the patient (such as the interview method) as part of the medication review.

The second most common pharmaceutical care issue flagged out derived from the same section in the GheOP^{3}S tool. This related to the fact that the community pharmacist does not question polypharmacy patients routinely about whether or not they have a medication chart. This question was only asked to those patients who were chronically taking five or more medications, as indicated in the GheOP^{3}S tool.

The third most common pharmaceutical care issue featuring in this study was a PPO investigating whether patients were covered seasonally by the influenza vaccine. It resulted that 35% of the participants do not take the vaccine on a regular basis and therefore these were educated by the pharmacist about the importance of being vaccinated accordingly, unless contraindicated. This same issue was found to be prevalent in two studies carried out in Belgium analysing the treatment of older patients, using the GheOP^{3}S tool, which both reported that 30% of the patients were not reminded to take the influenza vaccine (Tommelein et al., 2017; Kympers et al., 2019).

The study focused on one more pharmaceutical care issue from the general-care related items section related to the lack of OTC medication added in the patient's electronic record. One major drawback currently experienced in Maltese community pharmacies

is that pharmacists only have access to the last dispensed medication for patients availing themselves of the POYC service. This was not highly prevalent in the Belgian study by Tommelein et al. (2017) or the one by Foubert et al. (2020).

A common care issue brought up with the patients originated from a different GheOP^{3}S tool section looking into the prescription of potentially inappropriate drug classes, independent of diagnosis. Taking an antidepressant for a year or longer was flagged in nine of the patients participating in this research. This pharmaceutical care issue was reported as being more widespread in the study by Kympers et al. (2019), on a sample of Belgian patients only recently admitted in an acute geriatric ward, and in the study on a sample of Belgian patients living in ambulatory care (Tommelein et al., 2017).

Although most of the pharmaceutical care issues were implemented as pharmacist interventions, this was not always the case because some patients had multiple pharmaceutical care issues and a stepwise approach had to be adopted. This was the stage which required the pharmacist to adopt clinical judgement on which issues needed priority in clinical assessment.

The difference in the prevalence of the criterion relating to the prolonged use of antidepressants could be due to the diverse prescribing practices in different countries. In the local research 9 participants were on an antidepressant for a year or longer. The use of long-term psychiatric treatment in older patients is a subject that is often reported in literature (Percudani et al. 2005; Olfson et al., 2015; Gerlach et al., 2018) despite evidence illustrating the negative consequences associated with chronic antidepressant and benzodiazepine use such as the risks of falls and fractures (Lader et al., 2009;

Coupland et al., 2011; Janhsen et al., 2015). Factors which deter from the tapering of benzodiazepines and antidepressants comprise of inertia from the prescriber's part, the lack of doctor's insight on the problem, prescriber's lack of confidence in deprescribing and patient attitudes which resist change (Anderson et al., 2014).

Similarly the drug-drug interaction relating to oral antidiabetics/insulin and a cardioselective β-blocker applied to nine patients who took part in this local research. This was apparent in another community-based study where an 18% prevalence for this pharmaceutical care issue was reported (Tommelein et al., 2017).

There are several other important pharmaceutical care issues raised in the sample of patients under investigation. These included taking a specific drug despite the patient experiencing a side-effect or a condition which may exacerbate it, omission of treatment, drug-drug interactions, holistic care-related issues, prolonged duration of treatment and several PIMs.

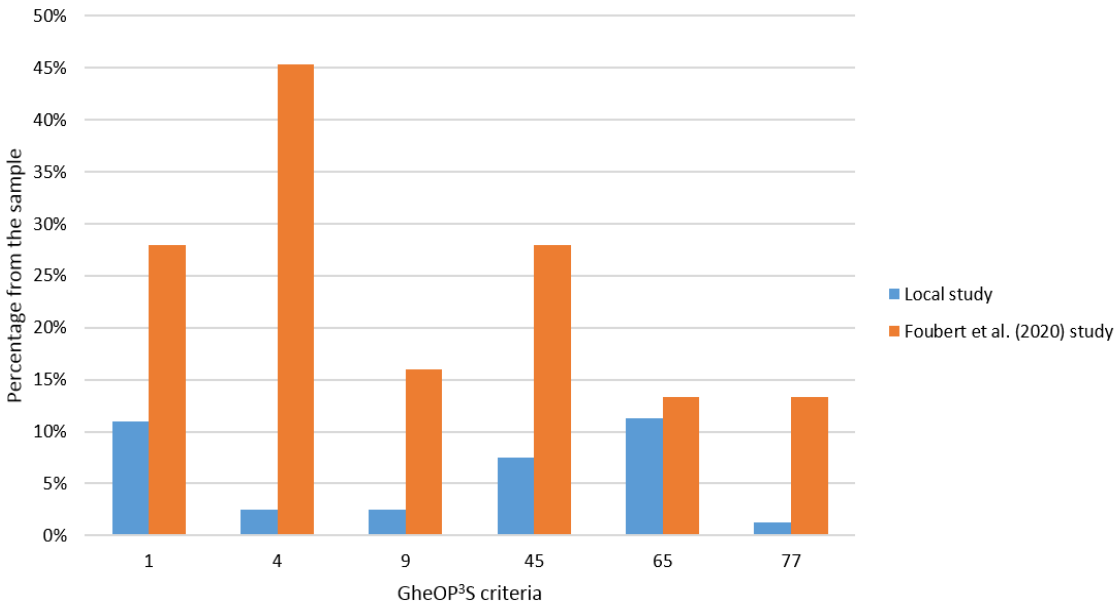
One of the criteria addressing issues with prolonged duration of treatment involved the use of "any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days". Such a criterion was deemed as highly prevalent in the two different Belgian studies (Kypmers et al., 2019; Foubert et al., 2020). This issue was flagged up in only 2 patients in this research i.e. it was not as prevalent as in the Belgian studies. Considering that the sample population size in the Maltese and Belgian studies were comparable, the determining factors of such a discrepancy could include the different prescribing trends between Maltese and Belgian doctors and the mean age of the sample cohort investigated (Table 4.1).

Table 4.1: Comparison between basic demographics of patients participating in similar studies using the GheOP^{3}S tool

	Kympers et al., 2019 Belgium	Foubert et al., 2020 Belgium	Malta study, 2021
Sample size (n)	60	75	80
Patients' mean age (years)	85.7	78.3	70.9

The omission of calcium/vitamin D supplementation in patients predisposed to osteoporosis was noted. The local research found that this is less prominent in the studied sample of patients than in the other two similar European studies on older patients. It turned out that all osteoporosis-prone patients were older females. This could be due to the fact that locally menopausal women are often and regularly referred for a bone density scan by their gynaecologist or GP and a number of patients were already on such supplements.

The bar graph in figure 4.1 was designed to delineate similarities and differences between the Foubert et al. (2020) study and this local research for the GheOP^{3}S pharmaceutical care issues detected. The results in the Foubert study (2020) only gave the percentages of the six most prevalent GheOP^{3}S criteria in their study and so one could not compare or contrast the results of the rest of the GheOP^{3}S criteria under evaluation. The predominant difference when comparing the two studies were the most prevalent pharmaceutical care issues. From the 6 commonest pharmaceutical care issues in the Foubert et al. (2020) study only two of these issues were among the most common in this study. These being "any antidepressant ≥ 1 year" and "oral antidiabetics/ insulin + cardioselective β-blocker".



Criterion no	GheOP^{3}S criterion description
1	Any antidepressant ≥ 1 year
4	Intermediate acting benzodiazepine or Z-drug at full dose/any dose for ≥ 30 subsequent days
9	PPI at full dose for ≥ 8 weeks
45	Elevated risk for osteoporosis and is not prescribed calcium/vitamin D
65	Oral antidiabetics/insulin + cardioselective β-blocker
77	combination of anticholinergic medications

Figure 4.1: Prevalence of GheOP^{3}S criteria between the two studies

It seems that the results obtained in the two studies do vary substantially in percentage prevalence except for GheOP^{3}S criterion number 65, regarding a specific drug-drug interaction. This could be due to the fact that in certain diabetic patients having a cardioselective β-blocker outweighs the risk of having hypoglycaemia, particularly if the patients have concurrent COPD or asthma, and therefore the use of a non-selective β-blocker is even riskier to the patient. Such a clinical dilemma is a recurrent problem in both countries as to-date there are no easy substitutes to β-blockers in disease states such as heart failure, arrhythmias and angina. The drug-drug interaction is still relevant but healthcare professionals need to provide patient education and monitoring to look out for glycaemic control. As the community pharmacist becomes aware of this drug-drug

interaction he/she is in a strategic position to encourage patients to self-monitor their blood glucose and educate the patients to always carry with them fast-acting glucose tablets in case they experience episodes of hypoglycaemia.

The comparative percentage prevalence of diabetes mellitus in both Belgium and Malta were noted to be 4.77% and 6.64% respectively (International Diabetes Federation, 2013) but the percentages of patients prescribed an oral antidiabetic/insulin and a cardioselective β-blocker concurrently were similar in the two studies. The reasons for this could be multifactorial such as different prescribing practices and prevalence of patients suffering from cardiovascular diseases and diabetes simultaneously.

4.3 Considerations on various aspects of pharmacist interventions

In this community-based study, it was found that the most common pharmacist interventions identified by the GheOP^{3}S tool were: checking the adherence to chronic medication, educating the patient about a specific condition or medication, recommending the influenza vaccine, listing OTC medication on an electronic record and providing a medication chart to polypharmacy patients.

The extent of adherence to chronic medication was evaluated in all patients in the first round of interviews and it seemed that all patients were still taking their recommended medication at the two-month follow-up stage. There could be links with the other pharmacist interventions carried out during the period of the study. Other factors contributing to adherence at two-month follow-up include aspects in pharmaceutical care plan being discussed with the patient, listing the patient's OTC medication on an electronic record so that an accurate account of the patient's treatment is available to the

pharmacist, patient education and the use of a medication schedule. Given that adherence was not known at the outset of the study, one cannot attribute the cause of such adherence at t = 2 months specifically to these interventions. What one can safely say is that in the follow-up all patients seemed to remain predominantly adherent to the prescribed treatment.

Another pharmacist intervention frequently employed in this study was patient education about a specific condition or medication. The specific conditions or medication referred to in this type of intervention originated from the GheOP^{3}S tool. Patient education consisted mainly in supporting participants with further information on their respective medication or condition and practical advice related to monitoring or self-monitoring.

The pharmacist's recommendations to older persons to get vaccinated against the seasonal influenza virus was in concordance with the public health's call to get vaccinated particularly this year in view of the COVID-19 pandemic. This was done in order to reduce the number of patients being admitted to hospital with influenza and therefore relieving the healthcare system from excessive pressure at such a delicate moment. This concept of emphasizing the need to take the influenza vaccine during this particular year was actually taken up internationally (Richmond et al., 2020).

One key pharmacist intervention was the creation of a database describing the treatment of all participants. This was done to overcome the limitation in Maltese community pharmacies whereby pharmacists only have access to the last dispensed free medication given through the POYC scheme, for patients registered with that particular pharmacy. Such an initiative to log the patients' treatments counteracts the lack of dispensing data,

particularly for the both OTC and prescription medications bought by patients at the community pharmacist's end. Having an updated complete list of treatment which the patient should be taking makes it easier for the pharmacist to propose a customised and holistic treatment optimisation for these older patients. This is related to the adherence pharmaceutical care issue treated earlier as it facilitated the pharmacist's promotion of adherence to chronic medication with the patients involved.

This study did not exclude patients who were not registered with the community pharmacy. Therefore a record for these patients was kept, together with those of the other patients, and this was particularly useful because this served as the only documentation available to the community pharmacist for this category of patients.

Polypharmacy patients who felt they would benefit from a medication schedule were given one by the researcher. In a review by Bonetti et al. (2018) the concept of providing a medication chart as part of a medication review prior to discharge from hospital was cited. In this paper it appears that the mention of a medication chart when patients are discharged from hospital was declining in more recent articles, indicating this intervention might be diminishing in relevance. One may highlight that the context of this community-based study is different and the use of a chart may still be recommendable as indicated by the GheOP^{3}S tool (Tommelein et al., 2016).

Other pharmacist interventions that were carried out in the first interview included referral to the doctor on the basis of several different considerations, patient monitoring, recommendations on the use of vitamins/drugs or their timings, alternative medication,

non-pharmacological approaches, advising on a customised pharmaceutical care plan and patient reassurance of pharmacist availability.

When one compares both methods of consultations in the two interviews carried out at baseline and in a span of two months, it was found that the follow-up was significantly shorter in duration than the first interview but more focused and straight to the point. It was also shown that there is a lower degree in variation, with respect to time, in the follow-up phase as opposed to the first interview. There seems to be a positive correlation between the lengths of interview in the two phases – the more time-consuming the first interview was, the lengthier the second interview was. This is reasonable considering that when a person has a number of issues to discuss in the first round, most of the issues indicated in the original encounter needed to be reviewed and re-evaluated in the second exercise.

With a general implementation rate of 79% for all pharmacist interventions carried out, one could safely deduce that the majority of the pharmacist interventions carried out were sustained after two months. In one of the Belgian studies (Foubert et al., 2020) an implementation rate of 33.3% was reported for "GheOP^{3}S-related DRPs". Such a disparity in implementation rate stems from the different modes of evaluating the interventions. A substantial number (77 out of a total of 190) of the interventions proposed in the local research were related to assessing medication adherence. Medication adherence was assessed differently in the study by Foubert et al (2020). Whilst the Belgian researchers measured adherence versus non-adherence, the researcher in the local research assessed discussing medication adherence at baseline versus maintaining it after two months. This is because in the local setting there is no

established system recording patient's adherence to treatment. This adherence pharmaceutical care issue comprised 41% of the total pharmacist recommendations in the first local medication review.

Results showed that the highest implementation rates were obtained in interventions involving maintaining adherence to chronic medication, referring to a doctor for a drug without an evidence-based indication, changing the timing of medications or vitamins, listing a patient's OTC medication on an electronic record and keeping up patient education about a specific condition or drug.

The more straightforward pharmacist recommendations, particularly those where the pharmacist could decide on alone (such as determining adherence to chronic medication, changing the timing of drugs or vitamins and listing a patient's OTC medication on an electronic record) were entirely implemented. This contrasted with other pharmacist recommendations such as adding a newly prescribed vitamin or drug which were implemented at a relatively lower successful rate.

It transpired that 14 patients who were commended the influenza vaccine actually took up the pharmacist's vaccine recommendation during the winter months. The rate of uptake could have been confounded with the public health's efforts to get older people vaccinated. The fact that during the period of investigation, the Department of Public Health was also advising everyone to get vaccinated for the seasonal influenza virus surely contributed to the concerted effort, undertaken at the pharmacy to promote such a recommendation with the patients involved. Patients who always take the influenza vaccine were not included with the pharmacist's recommendations neither at baseline

and nor after two months since their uptake would not have reflected the effect of the intervention itself.

Results show that a number of pharmacist interventions were not found to have been appropriately taken up after two months. These include the non-pharmacological approaches proposed for managing a condition, referrals to a doctor for a reduction in dose or for an underlying condition and safer alternative medication switch following referral to the doctor. The majority of these interventions relied on a prior visit to the family doctor to confirm any amendments. This feature could have been the main reason which deterred patients from responding to these interventions being suggested. It could be that the patient did not sufficiently understand the relevance and importance of the recommendation and might not have discussed it with his/her GP.

Another possible factor could be the reluctance from the physician's part to act upon the referral either in due consideration of the patient's overall wellbeing or because of apprehension from undesirable effects on the patient. Priority in clinical decision-making is also a factor that plays an important role in determining whether certain recommendations are taken up or not. For example a patient with sustained use of benzodiazepine and antidepressant normally requires two specific GheOP^{3}S recommendations - namely tapering down the benzodiazepine and removal of the antidepressant. Acting simultaneously on both recommendations may mean implementing too many changes on the patient at one go and applying two variables at a time is rarely advisable on scientific grounds. The best clinical decision would be to first taper down gradually the benzodiazepine (the riskier drug) before attempting to remove the antidepressant for the older patient concerned. This is why regular

medication reviews are important because with time more changes can be affected to fully optimise a patient's treatment. Similar considerations were also reflected upon in the paper by Foubert et al. (2020).

One more relevant aspect worth evaluating regarding the failure to realize certain pharmacist interventions was the fact that certain crucial changes or decisions were in the remit of a specialist rather than a GP. One specific example is a reconsideration on the need of a cardioselective β-blocker in a patient taking hypoglycaemic agents. Specialist appointments tend to be periodic, for example every six months, and therefore making it hard and highly unlikely for the patients to be realistically in touch with a specialist within the timeframe of the study.

The fact that one patient did not seek assistance from his GP or pharmacist did not necessarily mean that the patient concerned ignored the recommendation. Alternatively it could be that the patient might not have needed such services within this two-month time window.

The advice for another patient to start using his entitlement for the blood glucose meter was given at the follow-up phase, rather than at baseline. This occurred because the patient never mentioned that he was not monitoring his blood glucose levels, in the first encounter. Hence one could not analyse adherence to such a recommendation within the period of this research investigation.

In the clinical relevance exercise a number of relevant observations could be made. In case 1 there was unanimous agreement among healthcare professionals collaborating in

the study for all the pharmacist interventions carried out. These included patient education on sleep hygiene, patient education on anticholinergic side-effects due to a combination of anticholinergic drugs, influenza vaccine recommendation, checking the adherence to all chronic medication, provision of a clear medication schedule and listing the patient's OTC medication on an electronic record. One exception singled out from all intervention reviews was a disagreement by the majority of the pharmacists on the referral needed to reduce the dose of the drug lorazepam which contrasted with the GP's agreement with this pharmacist intervention.

For the second case, there was agreement between all healthcare professionals for a number of pharmacist interventions which included patient education on the use of osmotic laxatives when the patient is constipated (linked to the use of amlodipine), influenza vaccine recommendation, adherence to all chronic medication checked and listing the patient's OTC medication on an electronic record. Some level of disagreement was registered from one GP who contended that there was no need to monitor blood glucose levels in this non-insulin dependent diabetic patient and there was no need to educate the patient on possible changes in hypoglycaemia awareness, given that metformin does not usually cause hypoglycaemia.

The third case demonstrated agreement amongst all healthcare professionals on a number of pharmacist interventions such as patient education on possible changes in hypoglycaemia awareness due to metformin and sotalol being taken concurrently, influenza vaccine recommendation, checking the adherence for all chronic medication, listing patient's OTC medications on an electronic record and discussing features of pharmaceutical care that could be enhanced for the patient. There was only one GP who

expressed his disagreement on recommending monitoring of blood glucose levels to this patient. He justified his decision by claiming that "as per NICE guidelines we should not offer routine blood glucose self-monitoring unless the patient is on insulin or has had a hypoglycaemia episode, is operating heavy machinery or is planning to get pregnant."

There was widespread consensus among all healthcare professionals that the pharmacist interventions proposed were indeed clinically relevant. This is also in agreement with one of the Belgian studies which demonstrated that pharmacist interventions using the GheOP^{3}S tool were found to be valuable and crucial in improving medication optimisation in older patients (Kympers et al., 2019). The authors argued that using the GheOP^{3}S tool as part of a medication review helps to resolve PIP and explain further that if the GheOP^{3}S tool were to be applied on a routine basis, in primary care, a number of hospitalisations could be prevented.

4.4 Outcomes of the study

This study was a first for the local setting to explore feasibility of structured pharmacist intervention in community pharmacy setting through remote patient services. The study revealed that more pharmacist recommendations were carried out through telephone interviews when compared to those carried out in-person.

One of the main reasons might have been that some patients feel more at ease talking in the comfort of their own home and are more willing to cooperate and open up about their health. Another possible factor might have been that these patients were isolated and deprived of medical support for a long while during the COVID-19 pandemic (more likely to have received no or little medical assistance). A pharmacist intervention at this

point would have been direly needed. The higher standard deviation obtained after analysing the telephone interviews in the first interview, points towards the fact that such interviews were less streamlined with respect to time taken to carry them out. The fact that they were held over the telephone without any real or virtual face-to-face contact could have been one important limitation in this regard.

In the follow-up phase the mean number of pharmacist interventions implemented was the same for both forms of interviews, and resulted in the same extent of variation. This confirms that the interview mode did not affect the mean number of interventions implemented.

Such findings prove that there is an opportunity for this telepharmacy service to be consolidated and extended further. The service can be integrated with the newly inaugurated telemedicine hub, one of the latest initiatives taken by Maltese health authorities. Such a collaboration between healthcare professionals will extend the healthcare system to patients in need such as those with limited mobility, vulnerable, self-isolated or quarantined. Currently the telemedicine hub operates exclusively by primary care doctors who man the service round the clock[5] to support patients from all age groups. Results obtained in this research indicate that there is room for such a novel service to be amalgamated and supported by multidisciplinary healthcare professionals including pharmacists.

[5] Government of Malta. Telemedicine [Internet]. Valletta: Government of Malta; 2020 [cited 2021 May 7]. Available from: https://deputyprimeminister.gov.mt/en/phc/Pages/Services/Telemedicine/Telemedicine.aspx

A recent randomised control trial (Choudhry et al., 2018) demonstrated that remote clinical pharmacy advice improves medication adherence and risk of hospitalisation in patients suffering from diabetes, hyperlipidaemia and hypertension. Results show that this did not enhance disease management as indicated by laboratory markers (HbA1c, lipid profile and blood pressure) since the population studied was in a stable condition. Such a limitation has to be weighed in with the possibility of such patients having no pharmaceutical care at all, together with the fact that such a service may be improved upon and could be targeted for patients who are at a higher risk. A later study encourages the use of telepharmacy services to reach out to patients who were receiving no medication review follow-ups particularly throughout the COVID-19 pandemic (Koster et al., 2021).

The findings of the study contribute to the elaboration of a framework proposal for the implementation of community pharmacist services focused to the needs of older persons. A major shortcoming that can be seen in day-to-day practice is the insufficient, at times complete absence of, communication between hospitals and the pharmacy. The shortage of recent clinical data and discharge case summaries to the community pharmacist remains a missing essential link to ensure seamless transition of care. Having such data available will enhance the pharmacist's level of contribution to medication optimisation in the community. Currently a type 2a medication review could only be achieved but if more clinical data is presented to the community pharmacist a type 3 review can be undertaken.

The dispensing history available for medications dispensed through the local POYC scheme is certainly a step in the right direction but such a system can be further exploited

to provide more patient health information to be linked with the community pharmacy. The fact that there is no dispensing history for medications being purchased to be shared between pharmacies, or even within the same pharmacy, also hinders the pharmacists' knowledge of both the refill rate and consequently the patients' adherence to chronic medication.

Another positive aspect of the nationwide pharmaceutical service POYC scheme is that it offers a better opportunity for follow-up by the pharmacists of the patients registered with them. Albeit Maltese citizens tend to be loyal to their private GP (as seen also in the sample population analysed), a system for patients to be registered with one particular GP in both private and public entities could be the key in providing a more harmonious approach by their doctor. Having patients registered with one GP could pave the way for a more structured and customised primary healthcare system. Such an arrangement would unquestionably facilitate collaboration between the pharmacist and GP, enhance medication review services and promote essential medical follow-ups.

One another aspect worth citing is related to the latest revamping and relaunching of the "GheOP^{3}S-Tool Version 2", at the time of completion of this research (Foubert et al., 2021). Such a recent overhaul of the tool provided a means by which the GheOP^{3}S tool continues to be realistic and relevant in today's community pharmacy scenario. There are several differences worth noting from the previous tool to the newly revised version.

A total of 14 GheOP^{3}S criteria were added to the original tool whilst 17 others were deleted, mostly concerning PIMs and drug-drug interactions for older people. The updated version now incorporates the addendum consisting of drugs which should not

be used (or used with caution) in older persons with reduced renal function, which was published by Al Wazzan et al. (2018). Twelve recommendations which were deleted from the previous version due to their lack of relevance in the community pharmacy setting were not applicable to any of the patients in this study's sample. This confirms that these criteria were not pertinent according to the purpose of the GheOP^{3}S tool. For example an evidence-based decision had been made prior to initiating this research that it is no longer appropriate to consider DOACs as PIMs since evidence now shows that this is not the case. This proved to be one of the criteria which was deleted in this update.

One newly added criterion highlights the importance of the appropriate vaccination to patients with high risk of pneumococcal infection. This was a point which was mentioned by both pharmacists and doctors during the validation of the developed data collection tool. Such a consideration was disregarded at that time because it was not yet included in the older version of the GheOP^{3}S tool.

Further studies are now required on the newly updated GheOP^{3}S tool in order to assess its impact on patient outcomes. The fact that the first version of the GheOP^{3}S tool (Tommelein et al., 2016) was used in this study did not interfere with the overall progress and outcomes of the study. This is because the tool chosen was only used as a means to measure the feasibility and applicability of clinical tools to optimise patient's treatment in a community pharmacy setting which was achieved.

This study is a modest contribution by the researcher in view of the International Pharmaceutical Federation's slogan chosen for World Pharmacist's Day 2020 – the year

of data collection – "Transforming global health"[6]. The research was intended to transform the services given by community pharmacists to improve older patients' health outcomes and their quality of life in a bid to sew the seams in transitions of health care. The study was an exercise in pushing to the forefront the International Pharmaceutical Federation's development goals such as those relating to advancing integrated services, people-centred care and digital health namely goals 7, 15 and 20 respectively[7].

4.5 Strengths and limitations of the study

The study has several strengths namely the generalisability and relevance to the real world scenario. This includes the fact that the investigation was conducted with all types of patients, without excluding those who do not attend the pharmacy to avail themselves of the POYC services or patients who seek medical advice from one specific GP. A notable aspect of the study is the patient interview which provided an insight of the patient's experience on using the prescribed treatment and enabled the pharmacist to carry out a more personalised intervention.

Since the COVID-19 pandemic rendered a lot of vulnerable older persons housebound, the researcher had to cater for these patients via telephone consultations and this was in fact a strength of the study demonstrating resilience of the proposed service by maximising on remote pharmacist services. Through the remote services, the study

[6] Pharma Mirror. Pharmacists transforming global health is the focus of World pharmacists Day 2020 [Internet]. Bangladesh: PharmaMirror; 2020 [cited 2021 May 15]. Available from: https://www.pharmamirror.com/pharmacy/pharmacists-transforming-global-health-is-the-focus-of-world-pharmacists-day-2020/

[7] International Pharmaceutical Federation. FIP Development Goals [Internet]. Netherlands; International Pharmaceutical Federation; 2021 [cited 2021 May 15]. Available from: https://www.fip.org/fip-development-goals

captured patients with limited mobility who were unlikely to visit the pharmacy on their own. The inclusion of telephone consultations was an alternative effective means by which the pharmacist could support such patients, by extending the pharmaceutical services to the patients' households without face-to-face contact. This is altogether more meaningful in the context of the ongoing pandemic at a time when patients had doctor's appointments commonly cancelled, while others were afraid of attending clinics due to the risk of being infected with the COVID-19 virus.

Limitations of the study included the patient's medication history which relied solely on the individual patient's knowledge with the limited help of the POYC system which may not always show accurately what the patient is actually taking. The FRAX® score which measures risk for osteoporosis could not always be calculated appropriately for those patients who were interviewed remotely, provided that the patient's height and weight could only be roughly estimated by the patient concerned. Some of the patients encountered difficulty in memorising and relaying their pharmaceutical care issue/s to their doctor. Having multiple pharmacies and pharmacists participating in the study would provide greater generalisability to the outcome of the study.

Aspects of the Hawthorne effect (Sedgwick and Greenwood, 2015) could have been present during data collection. The latter limitation could have influenced some patients to change their behaviour because of their knowledge that they were participating in a study or to appease the healthcare professional. Furthermore it might be that the researcher could have performed better than in real-life situations.

One challenge when providing pharmaceutical intervention, was that any recommendation from the pharmacist's side was relayed to the physician through the

patient which reflects the current practice scenario. At times, this proved to be somewhat difficult particularly with those patients having poor medication literacy and/or limited communication. An explanatory note citing the evidenced-based suggestion from the pharmacist to the prescribing doctor or a meeting with the doctor would most probably be more efficient to counteract this problem. Whilst having a meeting between both the pharmacist and the GP would be ideal, this is rarely going to happen in real-life, and this is why this approach was not adopted in this study. The potential for the creation of future interdisciplinary medication reviews is very reasonable and healthcare professionals and policy makers should always strive to facilitate such a process for the benefit of the patient.

4.6 Recommendations for further studies

While the time period of two months was adequate to implement certain pharmacist interventions (like maintaining the adherence for chronic medication, uptake of the influenza vaccine and referrals to the doctor), other interventions such as convincing a patient that he/she should try alternative non-pharmacological approaches and evaluating whether they were effective in managing a condition could take more time for the patient to take up and/or experience the effect of the recommendation. If the study were to be continued for a longer time duration for example by including another follow-up in the space of four months from the first interview it could have resulted in higher implementation rates.

The findings related to the two methods of patient interviews are encouraging in the sense that telephone interviews still yielded positive implementation rates. If the study

were to be upscaled to include a higher participation of patients in the telephone medication review, it could further confer robustness to this mode of consultation.

It would be of interest to note the time dedicated to the preparatory phase of the medication review. One should also consider assessing all resources (including time and financial investment) required by the community pharmacist to carry out such an evaluation exercise, in a bid to further improve and optimise pharmaceutical care to the local community. In this regard a cost-effectiveness analysis would throw light on the sustainability of similar programs aimed at reaching a larger section of the population.

The very recent developments on the GheOP^{3}S tool version 2 confirm that such an explicit tool in medication optimisation is still relevant and has been refined and consolidated (Foubert et al., 2021). This revision introduced new criteria which were considered a priori by doctors and pharmacists when validating the data collection tool in this study whilst removing criteria which were not applicable to the patient cohort considered in this investigation. Any future studies in this area of clinical pharmacy should take into account the updated set of recommendations which provide principles which are more relevant to today's community pharmacy setting in European countries.

4.7 Conclusion

The results of this study suggest that the application of the GheOP³S tool in conjunction with the relevant developed data collection tool and patient interviews are feasible and applicable to the community pharmacy context, as part of a more comprehensive medication review. The clinical tools identified pertinent care issues in older patients

and facilitated pharmacist intervention. The data collection tool ensured a more accurate means of recording data and a more appropriate follow-up of the proposed interventions. The research aimed at enhancing the current pharmaceutical care service in the local community and confirming the GheOP³S tool as a standardised and effective method to identify care issues in polypharmacy patients. The evaluation focused on individual treatment optimisation within a community pharmacy setting. Priority to clinical issues that needed to be addressed had to be identified and this led to effective pharmacist intervention using the limited clinical data available to date to the local community pharmacist.

The study proved that a remote clinical pharmacy service was successful in implementing pharmacist interventions as much as face-to-face meetings was and there was no significant difference between the rate of implementation of the two methods of consultation. The study advocates for the set-up of remote clinical pharmacy services in primary care whereby community pharmacists can reach out to patients with reduced mobility or access to pharmacy services. This highly accessible service can be particularly exploited in unprecedented times and must be updated as technology and evidence continue to improve with time.

References

2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-94.

Al Wazzan AA, Tommelein E, Foubert K, Bonassi S, Onder G, Somers A, et al. Development and Application of the GheOP^{3}S-Tool Addendum on Potentially Inappropriate Prescribing (PIP) of Renally Excreted Active Drugs (READs) in Older Adults with Polypharmacy. Drugs Aging. 2018;35(4):343-64.

Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. BMJ Open. 2014;4(12).

Andreassen LM, Kjome RL, Sølvik UØ, Houghton J, Desborough JA. The potential for deprescribing in care home residents with Type 2 diabetes. Int J Clin Pharm. 2016;38(4):977-84.

Blenkinsopp A, Bond C, Raynor DK. Medication reviews. Br J Clin Pharmacol. 2012;74(4):573-80.

Bonetti AF, Reis WC, Lombardi NF, Mendes AM, Netto HP, Rotta I, et al. Pharmacist-led discharge medication counselling: A scoping review. J Eval Clin Pract. 2018;24(3):570-9.

Brandt J, Lê ML, Jantscher S, Bricelj A, Louizos C, Ng S, et al. Medication review service implementation in community pharmacy settings: Scoping review with focus on implementation studies. Res Social Adm Pharm. 2020;16(7):875-85.

Browne C, Kingston C, Keane C. Falls prevention focused medication review by a pharmacist in an acute hospital: implications for future practice. Int J Clin Pharm. 2014;36(5):969-75.

Chiu PK, Lee AW, See TY, Chan FH. Outcomes of a pharmacist-led medication review programme for hospitalised elderly patients. Hong Kong Med J. 2018;24(2):98-106.

Choudhry NK, Isaac T, Lauffenburger JC, Gopalakrishnan C, Lee M, Vachon A, et al. Effect of a remotely delivered tailored multicomponent approach to enhance medication taking for patients with hyperlipidemia, hypertension, and diabetes: the STIC2IT cluster randomized clinical trial. JAMA Intern Med. 2018;178(9):1182-9.

Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ. 2011;343:d4551.

Curtin D, Jennings E, Daunt R, Curtin S, Randles M, Gallagher P, et al. Deprescribing in older people approaching end of life: a randomized controlled trial using STOPPFrail criteria. JAGS. 2020;68(4):762-9.

Dimitrow MS, Airaksinen MS, Kivela SL, Lyles A, Leikola SN. Comparison of prescribing criteria to evaluate the appropriateness of drug treatment in individuals aged 65 and older: a systematic review. J Am Geriatr Soc. 2011;59(8):1521-30.

Easter JC, DeWalt DA. The medication optimization value proposition: Aligning teams and education to improve care. N C Med J. 2017;78(3):168-72.

Farley JF, Ferreri SP, Easter JC, McClurg MR. The North Carolina experiment: active research in the development and assessment of new practice models. N C Med J. 2017;78(3):186-90.

Fenech Caruana T. Medication use management in a long-term elderly care setting [dissertation]. Msida (Malta): Department of Pharmacy, University of Malta. 2018.

Foubert K, Mehuys E, Maesschalck J, De Wulf I, Wuyts J, Foulon V, et al. Pharmacist-led medication review in community-dwelling older patients using the GheOP^{3}S-tool: General practitioners' acceptance and implementation of pharmacists' recommendations. J Eval Clin Pract. 2020;26(3):962-72.

Foubert K, Capiau A, Mehuys E, De Bolle L, Somers A, Petrovic M, et al. Ghent Older People's Prescriptions Community Pharmacy Screening (GheOP^{3}S)-Tool Version 2: Update of a Tool to Detect Drug-Related Problems in Older People in Primary Care. Drugs Aging. 2021:1-11.

Gauci M, Wirth F, Azzopardi LM, Serracino-Inglott A. Clinical pharmacist implementation of a medication assessment tool for long-term management of atrial fibrillation in older persons. Pharm Pract (Granada). 2019;17(1):1349.

Gauci M, Wirth F, Camilleri L, Azzopardi LM, Serracino-Inglott A. Design and application of a medication assessment tool for secondary prevention of stroke. Int J Clin Pharm. 2017;39(5):1008-12.

Gauci M, Wirth F, Camilleri L, Azzopardi LM, Serracino-Inglott A. Assessing appropriateness of drug therapy in older persons: Development and application of a medication assessment tool for long-term management of atrial fibrillation. Pharm Pract (Granada). 2017;15(4):1021.

Gerlach LB, Wiechers IR, Maust DT. Prescription benzodiazepine use among older adults: a critical review. Harv Rev Psychiatry. 2018;26(5):264-273.

Griese-Mammen N, Hersberger KE, Messerli M, Leikola S, Horvat N, van Mil JF, et al. PCNE definition of medication review: reaching agreement. Int J Clin Pharm. 2018;40(5):1199-208.

Hanlon JT, Schmader KE. The medication appropriateness index at 20: where it started, where it has been, and where it may be going. Drugs Aging. 2013;30(11):893-900.

Houlind MB, Andersen AL, Treldal C, Jørgensen LM, Kannegaard PN, Castillo LS, et al. A collaborative medication review including Deprescribing for older patients in an emergency department: a longitudinal feasibility study. J Clin Med. 2020;9(2):348.

Huiskes VJ, Burger DM, van den Ende CH, van den Bemt BJ. Effectiveness of medication review: a systematic review and meta-analysis of randomized controlled trials. BMC Fam Pract. 2017;18(1):5.

International Diabetes Federation. IDF Diabetes Atlas. 6th ed. Brussels: International Diabetes Federation; 2013.

Janhsen K, Roser P, Hoffmann K. The problems of long-term treatment with benzodiazepines and related substances: Prescribing practice, epidemiology, and the treatment of withdrawal. Dtsch Arztebl Int. 2015;112(1-2):1-7.

Koster ES, Philbert D, Bouvy ML. Impact of the COVID-19 epidemic on the provision of pharmaceutical care in community pharmacies. Res Social Adm Pharm. 2021;17(1):2002-4.

Kretchy IA, Asiedu-Danso M, Kretchy JP. Medication management and adherence during the COVID-19 pandemic: perspectives and experiences from low-and middle-income countries. Res Social Adm Pharm. 2021;17(1):2023-6.

Kympers CE, Tommelein E, Van Leeuwen E, Boussery K, Petrovic M, Somers A. Detection of potentially inappropriate prescribing in older patients with the GheOP³S-tool: completeness and clinical relevance. Acta Clinica Belgica. 2019;74(2):126-36.

Jokanovic N, Tan EC, Sudhakaran S, Kirkpatrick CM, Dooley MJ, Ryan-Atwood TE, et al. Pharmacist-led medication review in community settings: an overview of systematic reviews. Res Social Adm Pharm. 2017;13(4):661-85.

Lader M, Tylee A, Donoghue J. Withdrawing benzodiazepines in primary care. CNS drugs. 2009;23(1):19-34.

Lee JK, Alshehri S, Kutbi HI, Martin JR. Optimizing pharmacotherapy in elderly patients: the role of pharmacists. Integr Pharm Res Pract. 2015;4:101-111.

Lenander C, Bondesson Å, Viberg N, Beckman A, Midlöv P. Effects of medication reviews on use of potentially inappropriate medications in elderly patients; a cross-sectional study in Swedish primary care. BMC Health Serv Res. 2018;18(1):1-9.

Lim WS, Low HN, Chan SP, Chen HN, Ding YY, Tan TL. Impact of a pharmacist consult clinic on a hospital-based geriatric outpatient clinic in Singapore. Ann Acad Med Singap. 2004;33(2):220-7.

Lindsay J, Dooley M, Martin J, Fay M, Kearney A, Khatun M, Barras M. The development and evaluation of an oncological palliative care deprescribing guideline: the 'OncPal deprescribing guideline'. Support Care Cancer. 2015;23(1):71-8.

Liu S, Luo P, Tang M, Hu Q, Polidoro JP, Sun S, Gong Z. Providing pharmacy services during the coronavirus pandemic. Int J Clin Pharm. 2020;42(2):299-304.

Malet-Larrea A, Goyenechea E, Gastelurrutia MA, Calvo B, García-Cárdenas V, Cabases JM, et al. Cost analysis and cost-benefit analysis of a medication review with follow-up service in aged polypharmacy patients. Eur J Health Econ. 2017;18(9):1069-78.

Marcum ZA, Hanlon JT, Murray MD. Improving medication adherence and health outcomes in older adults: an evidence-based review of randomized controlled trials. Drugs Aging. 2017;34(3):191-201.

Martin P, Tamblyn R, Benedetti A, Ahmed S, Tannenbaum C. Effect of a pharmacist-led educational intervention on inappropriate medication prescriptions in older adults: the D-PRESCRIBE randomized clinical trial. JAMA. 2018;320(18):1889-98.

Milos V, Rekman E, Bondesson Å, Eriksson T, Jakobsson U, Westerlund T, et al. Improving the quality of pharmacotherapy in elderly primary care patients through medication reviews: a randomised controlled study. Drugs Aging. 2013;30(4):235-46.

Milosavljevic A, Aspden T, Harrison J. Community pharmacist-led interventions and their impact on patients' medication adherence and other health outcomes: a systematic review. Int J Pharm Pract. 2018;26(5):387-97.

Molokhia M, Majeed A. Current and future perspectives on the management of polypharmacy. BMC Fam Pract. 2017;18(1):1-9.

National Institute for Health and Care Excellence. Preventing stroke in people with atrial fibrillation - NICE Pathway [Internet]. London: NICE; 2021 [cited 2021 Apr 27]. Available from: https://pathways.nice.org.uk/pathways/atrial-fibrillation/preventing-stroke-in-people-with-atrial-fibrillation#content=view-node:nodes-anticoagulation

Nicieza García ML, Salgueiro Vázquez E, Jimeno Demuth FJ, Manso Rodríguez G. Beers versus STOPP criteria in polyharmacy community-dwelling older patients. Farmacia Hospitalaria. 2016;40(3):150-64.

Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. JAMA Psychiatry. 2015;72(2):136-42.

O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015;44(2):213-8.

Pan KL, Singer DE, Ovbiagele B, Wu YL, Ahmed MA, Lee M. Effects of non–vitamin K antagonist oral anticoagulants versus warfarin in patients with atrial fibrillation and valvular heart disease: a systematic review and meta-analysis. J Am Heart Assoc. 2017;6(7):e005835.

Percudani M, Barbui C, Fortino I, Petrovich L. Antidepressant drug prescribing among elderly subjects: a population-based study. Int J Geriatr Psychiatry. 2005;20(2):113-8

Pereira KG, Peres MA, Iop D, Boing AC, Boing AF, Aziz M, et al. Polypharmacy among the elderly: a population-based study. Rev Bras Epidemiol. 2017;20:335-44.

Pharmaceutical Care Network Europe (PCNE). Position paper on the PCNE definition of Medication Review 2016. [Internet] 2016 Apr [cited 2021 Mar 18]. Available from: https://www.pcne.org/upload/files/149_Position_Paper_on_PCNE_Medication_Review_final.pdf.

Royal Pharmaceutical Society. Medicines Optimisation: Helping patients to make the most of medicines. [Internet] 2013 May [cited 2021 Feb 12]. Available from: https://www.nhs.uk/about-the-nhs-website/professionals/healthandcareprofessionals/your-pages/documents/rps-medicines-optimisation.pdf

Reeve E. Deprescribing tools: a review of the types of tools available to aid deprescribing in clinical practice. J. Pharm. Pract. Res. 2020;50(1):98-107.

Richmond H, Rees N, McHale S, Rak A, Anderson J. Seasonal influenza vaccination during a pandemic. Hum Vacc Immunother. 2020;16(9):2219-21.

Riordan DO, Walsh KA, Galvin R, Sinnott C, Kearney PM, Byrne S. The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review. SAGE Open Med. 2016;4:1-18.

Sedgwick P, Greenwood N. Understanding the Hawthorne effect. BMJ. 2015;351:h4672.

Shelton PS, Fritsch MA, Scott MA. Assessing medication appropriateness in the elderly. Drugs Aging. 2000;16(6):437-50.

Sommerauer C, Schlender L, Krause M, Weissbach S, Rieckert A, Martinez YV, et al. Effectiveness and safety of vitamin K antagonists and new anticoagulants in the prevention of thromboembolism in atrial fibrillation in older adults–a systematic review of reviews and the development of recommendations to reduce inappropriate prescribing. BMC Geriatr. 2017;17(1):73-98.

Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet. 2007;370(9582):173-84.

Stojanović M, Vuković M, Jovanović M, Dimitrijević S, Radenković M. GheOP^{3}S tool and START/STOPP criteria version 2 for screening of potentially inappropriate medications and omissions in nursing home residents. J Eval Clin Pract. 2020;26(1):158-64.

Tommelein E, Petrovic M, Somers A, Mehuys E, van der Cammen T, Boussery K. Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S) tool. J Public Health (Oxf). 2016;38(2):e158-70.

Tommelein E, Mehuys E, Van Tongelen I, Petrovic M, Somers A, Colin P, et al. Community pharmacists' evaluation of potentially inappropriate prescribing in older community-dwelling patients with polypharmacy: observational research based on the GheOP³S tool. J Public Health (Oxf). 2017;39(3):583-92.

Tsuyuki RT, Al Hamarneh YN, Jones CA, Hemmelgarn BR. The effectiveness of pharmacist interventions on cardiovascular risk: the multicenter randomized controlled RxEACH trial. J Am Coll Cardiol. 2016;67(24):2846-54.

Appendices

Appendix 1: Developed community pharmacy data collection tool (part 1)

Patient Profile	
Patient code number	
Number of medications	
List of medications	
Age	
Sex	
Chronic conditions	
Private or public GP service?	
Face-to-face or telephone meeting?	

Pharmaceutical care issues		**Tick box**	**Effectiveness and Sustainability of Pharmacist Intervention**		**Tick box**
Code	Time = 0		Code	Time = 2 months	
A1.	Prolonged drug treatment – referral to GP/specialist		A2.	Appointment fixed with GP/specialist	
B1.	Drug prescribed without an evidence-based indication – referral to GP/specialist		B2.	Patient took up the referral recommendation and sought medical advice – patient stopped treatment	
C1.	Consider non-pharmacological approach		C2.	Non-pharmacological approach was effective in managing a condition	
D1.	Referral to GP/specialist depending on underlying condition		D2	Patient took up the referral recommendation and sought medical advice – better management of medical condition	
E1.	Verify with GP/specialist		E2.	Review of any changes in the past 2 months	

Pharmaceutical care issues		**Tick box**	**Effectiveness and Sustainability of Pharmacist Intervention**		**Tick box**
Code	Time = 0		Code	Time = 2 months	
F1.	Check if step-up approach was considered and adopted		F2.	Patient took up the referral recommendation and sought medical advice – patient reduced dose	
G1.	Safer alternative medication available – referral to GP/specialist		G2.	Patient took up the referral recommendation and sought medical advice – safer alternative medication was prescribed	
H1.	Safer alternative medication available – medication switch recommended by pharmacist		H2.	Patient is satisfied with the safer alternative provided by the pharmacist	
I1.	Monitoring need		I2.	Monitoring need	
J1.	Start drug at lowest possible dose		J2.	Patient took up the referral recommendation and sought medical advice – patient reduced dose	
K1.	Reduce dose – referral to GP/specialist		K2.	Patient took up the referral recommendation and sought medical advice – patient reduced dose	
L1.	Addition of another drug needed – referral to GP/specialist		L2.	Patient took up the referral recommendation and sought medical advice – new drug added	
M1.	Addition of another drug/vitamins recommended by pharmacist		M2.	Patient still takes the other medication/vitamin recommended by the pharmacist	
N1.	Omission of drug/vitamin recommended by pharmacist		N2.	Patient omitted a drug/vitamin as recommended by the pharmacist	

Appendix 1: Developed community pharmacy data collection tool (part 3)

Pharmaceutical care issues		**Tick box**	**Effectiveness and Sustainability of Pharmacist Intervention**		**Tick box**
Code	Time = 0		Code	Time = 2 months	
O1.	Guidance on timing of medications/ vitamins		O2.	Patient is taking medications/ vitamins at the appropriate timings	
P1.	Patient education		P2.	Patient education was maintained	
Q1.	Discuss with GP/specialist		Q2.	Discussion with GP/specialist led to change in pharmaceutical care plan	
R1.	Influenza vaccine recommendation		R2.	Patient took up influenza vaccine	
S1.	Recommend assistance in medication/health issues (by nurse, neighbour, relatives etc) in frail older patients or older patients with reduced cognition		S2.	Patient acquired assistance in medication/health issues	
T1.	Aspects of pharmaceutical care that could be improved for the patient were discussed		T2.	Change in pharmaceutical care plan was effective for the patient	
U1.	Adherence for all chronic medication was checked or discussed (e.g. through refill rate) for the past year		U2.	Further change in pharmaceutical care plan was recommended	
V1.	Polypharmacy patients (chronically taking 5 or more drugs) were provided with a clear medication schedule		V2.	Patient is using the clear medication schedule provided	

Appendix 1: Developed community pharmacy data collection tool (part 4)

Pharmaceutical care issues		**Tick box**	**Effectiveness and Sustainability of Pharmacist Intervention**		**Tick box**
Code	Time = 0		Code	Time = 2 months	
W1.	Patient had OTC medication not listed on the patient's electronic record.		W2.	Patient's electronic record was updated to include all drugs and vitamins.	
X1.	Other pharmaceutical intervention not listed above:		X2	Other pharmaceutical intervention not listed above:	
	Interview time:		Interview time:		

Appendix 2: University Research Ethics Committee approval

L-Università ta' Malta

Tiziana Fenech Caruana <tiziana.fenech-caruana.13@um.edu.mt>

PharmD thesis ethics submission

3 messages

Tiziana Fenech Caruana <tiziana.fenech-caruana.13@um.edu.mt> 31 July 2020 at 12:27
To: research-ethics.ms@um.edu.mt
Cc: "Lilian M. Azzopardi" <lilian.m.azzopardi@um.edu.mt>

To whom it may concern,

Kindly find attached my UREC form for RECORDS purposes and relevant documents for my Doctorate in Pharmacy dissertation entitled "Medication optimisation in older patients". My academic supervisor Prof Lilian M. Azzopardi is cced to endorse these documents.

Thanks and kind regards,
Tiziana Fenech Caruana
Pharmacist and PharmD student

2 attachments

UREC FORM V_15062020 6156 (1).pdf
92K

Documents.zip
2098K

Lilian M Azzopardi <lilian.m.azzopardi@um.edu.mt> 3 August 2020 at 11:17
To: FACULTY RESEARCH AND SURGERY <research-ethics.ms@um.edu.mt>
Cc: Tiziana Fenech Caruana <tiziana.fenech-caruana.13@um.edu.mt>

Application endorsed

regards

Lilian

Lilian M. Azzopardi
Professor and Head, Department of Pharmacy
University of Malta
President, European Association of Faculties of Pharmacy

[Quoted text hidden]

FACULTY RESEARCH ETHICS COMMITTEE <research-ethics.ms@um.edu.mt> 3 August 2020 at 12:34
To: Tiziana Fenech Caruana <tiziana.fenech-caruana.13@um.edu.mt>
Cc: Lilian M Azzopardi <lilian.m.azzopardi@um.edu.mt>

Dear Tiziana Fenech Caruana,

Since your self-assessment resulted in no issues being identified, FREC will file your application for record and audit purposes but will not review it.

Any ethical and legal issues including data protection issues are your responsibility and that of your supervisor.

L-Università ta' Malta

Ruth Stivala | Secretary
B.A.(Hons)(Melit.),M.A.(Melit.)

Faculty Research Ethics Committee
Faculty of Medicine and Surgery
Medical School, Mater Dei Hospital
+356 2340 1214

https://www.um.edu.mt/ms/students/researchethics

Appendix 3: Templates of medication schedules used with the patients

MALTESE VERSION

Isem u kunjom: _____

Mediċina	**Filgħodu**	**F'nofsinhar**	**Filgħaxija**

Data ta' reviżjoni: _____

ENGLISH VERSION

Name and surname: _____

Medicine	**Morning**	**Noon**	**Evening**

Revision date: _____

Appendix 4A: GheOP^{3}S Tool (Tommelein et al., 2016)

Part 1a: Potentially inappropriate drugs, independent of diagnosis – drug classes

No.	Item	Alternative
1	Any antidepressant ≥1 year	Check if indication is still present, if not: discontinue therapy If therapy is continued: check co-medication
2	Any antipsychotic drug ≥1 month	First, consider need for chronic use (≈ Is original indication still present?), if not: discontinue therapy Second, always consider non-pharmacological approach
3	Any drug for arterial vascular disorders	Therapeutic abstention Recommend non-pharmacological approach (compression hosiery, discuss referral to surgery with GP, physiotherapy. . .).
4	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days	– For sleeping disorders: Start-up: First, consider non-pharmacological approach Second, prefer intermediate acting benzodiazepine or Z-product at 1/2 dose of young adults >30 subsequent days: consider non-pharmacological approach (sleep hygiene), provide GP with withdrawal plan and assure GP of support by pharmacists in withdrawal – For anxiety: consider non-pharmacological approach and switching to SSRI
5	Any short- or long-acting benzodiazepine	– Start-up: First, consider non-pharmacological approach Second, Prefer intermediate acting benzodiazepine or Z-product at 1/2 dose of young adults <30 subsequent days – Chronic: consider non-pharmacological approach (sleep hygiene), provide GP with withdrawal plan and assure GP of support by pharmacists in withdrawal
6	Any long-acting sulfonylurea derivative	Metformin or any short-acting sulfonylurea derivative
7	Any nasal vasoconstrictor ≥ 1 month	Hypertonic saline solution or referral to GP

Part 1a: Potentially inappropriate drugs, independent of diagnosis – drug classes (cont'd)

No.	Item	Alternative
8	Any oral NSAID	Consider need for anti-inflammatory therapy. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice If therapy is considered necessary, prefer low dose ibuprofen. Avoid NSAIDs with high GI-risk (piroxicam, ketorolac) Prefer ibuprofen/naproxen when CV-risk Prefer NSAIDs with short half-life (ibuprofen, diclofenac) Always add gastroprotection (most evidence for PPI in standard dose) Closely monitor renal function or blood pressure depending on present diagnoses
9	Any PPI at full dose ≥8 weeks	Consider need for chronic use and reduce dose if possible
10	Any recently marketed drug (black triangles)	Consider using drug with similar indication and more evidence in older patients
11	Any sedating antihistaminic drug	First, verify indication, if not valid: stop therapy or switch to appropriate therapy Second, if indication is valid: switch to non-sedating antihistaminic drug

Part 1b: Potentially inappropriate drugs, independent of diagnosis – specific molecules

No.	Item	Alternative
12	Alizapride	Non-pharmacological approach, if not sufficient: reduce dose to 3 × 25 mg/day
13	Bisacodyl	Macrogol/lactulose
14	Clonidine	Consider other safer antihypertensive
15	Codeine and its derivatives for acute cough	Therapeutic abstention or safer alternative (e.g. honey)
16	Dabigatran	Warfarin/acetylsalicylic acid/heparin, depending on indication

Part 1b: Potentially inappropriate drugs, independent of diagnosis – specific molecules (cont'd)

No.	Item	Alternative
17	Digoxin > 0.125mg/day	Digoxin ≤0.125 mg/day or serum level between 0.5 and 0.8 µg/l
18	Dipyridamole monotherapy (without aspirin)	Acetylsalicylic acid in low dose
19	Ginkgo biloba or Panax ginseng	Referral depending on underlying condition
20	Liquid paraffin	Macrogol/lactulose
21	Methyldopa	Consider other safer antihypertensive
22	Metoclopramide	Non-pharmacological approach, if not sufficient: reduce dose to 3 × 5 mg/day
23	Pentazocine	Consider paracetamol/codeine combination or pure morphinomimetic agent, depending on indication
24	Phenobarbital	Verify that GP checked diagnosis with prescribing neurologist
25	Pseudoephedrine oral	Short-term intranasal therapy (nasal vasoconstrictor <7 days or hypertonic saline solution)
26	Rivaroxaban or apixaban	Warfarin/acetylsalicylic acid/heparin, depending on indication
27	Senna glycosides	Macrogol/lactulose
28	Picosulfate	Macrogol/lactulose
29	Theophylline	Reconsider indication, preferably stop theophylline
30	Ticlopidine, new prescription	Verify indication, prefer safer alternative
31	Tramadol, new prescription	Check if step-up approach was used. Paracetamol/codeine could be more appropriate

Part 2a: Potentially inappropriate drugs, dependent on diagnosis – drug classes

No.	Item	Alternative
32	Any antipsychotic other than quetiapine and clozapine with Parkinson's disease	Quetiapine and clozapine are preferred: they appear to be less likely to precipitate worsening of Parkinson's disease
33	Anticholinergics (e.g. antihistamines, antidepressants, antipsychotics and antispasmodics) with dementia or cognitive impairment	Consider drug for same indication with less or none anticholinergic activity
34	Anticholinergics (e.g. antihistamines, antidepressants, antipsychotics and antispasmodics) with constipation	Consider drug for same indication with less or none anticholinergic activity If therapy is necessary: add osmotic laxative and apply non-pharmacological measures
35	Anticholinergics with benign prostatic hypertrophy	Consider drug for same indication with less or none anticholinergic activity If therapy is necessary: check urinary residue shortly after start with anticholinergic drug. Recheck when suspicion of urine retention
36	Calcium channel blockers with constipation	Prefer class of antihypertensive agent that has not constipation as side effect If calcium channel blocker is necessary, prefer dihydropyridines (amlodipine) and/or add osmotic laxative
37	Non-selective β-blockers with asthma or COPD	Consider cardioselective β-blocker or other class of antihypertensive drugs
38	Oral corticosteroids > 1 week with diabetes	Closely monitor glycaemic control and blood pressure Shorten therapy duration as much as possible Always warn patient about possible dysregulation
39	Oral corticosteroids > 1 week with hypertension	Closely monitor blood pressure and glycaemic control Shorten therapy duration as much as possible Always warn patient about possible dysregulation
40	Thiazide and loop diuretics with gout	Prefer other class of antihypertensive drugs If diuretic is necessary, prefer potassium sparing (pay attention to renal impairment and probable interactions)

Part 2b: Potentially inappropriate drugs, dependent on diagnosis – specific molecules

No.	Item	Alternative
41	Alizapride with Parkinson's disease	First, always apply non-drug and diet therapy. Second, if anti-emetic therapy is necessary, prefer domperidone in low dose only if no cardiac risk factors are present and no other QT-prolonging drugs are used
42	Metoclopramide with Parkinson's disease	First, always apply non-drug and diet therapy. Second, if anti-emetic therapy is necessary, prefer domperidone in low dose only if no cardiac risk factors are present and no other QT-prolonging drugs are used

Part 3: PPOs

No.	Item
43	The patient is taking an equivalent of 7.5mg of oral prednisone or more for ≥ 3 months and is not prescribed calcium/vitamin D supplementation and bisphosphonates.
44	The patient is taking narcotic analgesics and is not prescribed appropriate preventative bowel regimen (preferably macrogol or lactulose).
45	The patient has an elevated risk for osteoporosis (determined via FRAX tool) and is not prescribed calcium/Vitamin D supplementation.
46	The patient is taking oral corticosteroids for ≥ 1 month and is not prescribed calcium/vitamin D supplementation.
47	The patient is not reminded and proposed to undergo yearly influenza vaccination.
48	The patient is taking methotrexate and is not prescribed folic acid supplementation.

Part 4: Drug-drug interactions of specific relevance

No	Item	Alternative
49	Vitamin K antagonists (VKA) + oral NSAIDs	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice Second, if NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
50	RAAS inhibitor + potassium sparing diuretic/ potassium supplements/potassium containing drugs	First, preferably change to non-potassium sparing diuretic/switch to non-potassium containing drug equivalent Second, if combination is unavoidable: monitor renal function and serum potassium and always inform patient about symptoms of hyperkalaemia
51	VKA + antiplatelet drugs (especially aspirin), unless prescribed by internist/cardiologist	First, check if combination is appropriate (artificial valve, up to 3 months after acute coronary syndrome and for rheumatic mitral valve stenosis) Second, when combination is not appropriate: stop aspirin and monitor INR
52	VKA + trimethoprim/sulfamethoxazole (TMP/SMX)	First, preferably switch to other antibiotic based on indication Second, if combination is unavoidable: monitor INR
53	Oral NSAID + oral corticosteroids	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice Second, if NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
54	Oral NSAID + diuretic	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice Second, if NSAID is unavoidable: monitor renal function, blood pressure and serum potassium

Part 4: Drug-drug interactions of specific relevance (cont'd)

No	Item	Alternative
55	Digoxin + macrolide antibiotics	First, preferably switch to other antibiotic based on indication Second, if combination is unavoidable: monitor serum digoxin levels and always inform patient about signs of digoxin toxicity
56	Digoxin + verapamil/diltiazem	First, starting digoxin: use lowest possible dose Second, starting diltiazem: check serum digoxin levels for 1–2 weeks 3rd Starting verapamil: lower digoxin dose to 50–70% of usual dose + check serum digoxin levels for 1–2 weeks 4th Altering dose of verapamil/diltiazem: alter digoxin dose using serum digoxin levels Always inform patient about signs of digoxin toxicity
57	Lithium + RAAS inhibitors	First, consider need for RAAS inhibitor Second, if combination is unavoidable: monitor lithium levels within 3–5 days after starting RAAS inhibitor and always inform patient about signs of lithium toxicity
58	Lithium + oral NSAID	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice Second, if combination is unavoidable: determine lithium levels before starting NSAID, give NSAID with strict schedule, check lithium levels after 3 days and modify intake dosage. Act similarly when NSAID is stopped and always inform patient about signs of lithium toxicity
59	Lithium + diuretics	First, consider need for diuretic. If possible: replace with appropriate alternative. Second, if combination is unavoidable: determine lithium levels before starting diuretic, avoid 'on demand' use of diuretic, determine lithium levels after 3 days and modify intake dosage. Act similarly when diuretic is stopped and always inform patient about signs of lithium toxicity

Part 4: Drug-drug interactions of specific relevance (cont'd)

No	Item	Alternative
60	Theophylline + quinolones/macrolides	First, consider switching to other antibiotic based on indication Second, if combination is unavoidable: monitor theophylline levels and always consider stopping theophylline
61	RAAS inhibitor + oral NSAID	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice. Second, if NSAID is unavoidable: monitor renal function, blood pressure and serum potassium
62	Oral NSAID + selective serotonin reuptake inhibitor/serotonin and noradrenaline reuptake inhibitor	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice Second, if NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
63	RAAS inhibitor + TMP/SMX	First, preferably switch to other antibiotic based on indication Second, if combination is unavoidable: monitor renal function and potassium level
64	Oral antidiabetics/insulin + non-selective β-blocker	First, always change to cardioselective β-blocker (also relevant for eye drops) Second, inform patient about possible changes in awareness of hypoglycaemia
65	Oral antidiabetics/insulin + cardioselective β-blocker	First, consider need for β-blocker + check glycaemic control Second, inform patient about possible changes in awareness of hypoglycaemia
66	Alprazolam/midazolam/triazolam/zolpidem/zopiclone + strong CYP3A4 inhibitor	First, preferably stop benzodiazepine use during treatment with CYP3A4 inhibitor Second, switch to equivalent drug with less or without CYP3A4 inhibiting activity
67	Calcium channel blocker + strong CYP3A4 inhibitor	Preferably switch to equivalent drug with less or without CYP3A4 inhibiting activity

Part 4: Drug-drug interactions of specific relevance (cont'd)

No	Item	Alternative
68	Oral NSAID + antiplatelet drugs	First, consider need for NSAID. If possible: paracetamol or stronger non-NSAID (e.g. opioid) is safer choice Second, if NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
69	Phenytoin + TMP/SMX	First, preferably switch to other antibiotic based on indication Second, if combination is unavoidable: monitor phenytoin levels
70	First dose RAAS inhibitor at full dosage + pretreatment with diuretic	First, start RAAS inhibitor in lowest possible dose for 3 days Second, always give RAAS inhibitor first 3 days at night and diuretic in the morning 3rd Always inform patient about possible orthostatic effect
71	Tamoxifen + strong CYP2D6 inhibitors	Prefer equivalent drug with less or without CYP2D6 inhibiting activity
72	Calcium + quinolones/tetracyclines	First, use calcium minimum 2 h after quinolone/tetracycline or take quinolone/tetracycline 6 h after intake of calcium Second, if not possible: stop calcium
73	Calcium + strontium ranelate	First, use calcium minimum 2 h after strontium ranelate or take strontium ranelate 6 h after intake of calcium Second, if not possible: stop calcium
74	Calcium + levothyroxine	First, use calcium minimum 2 h after levothyroxine drug or take levothyroxine 6 h after intake of calcium Second, if not possible: stop calcium
75	Bisphosphonate + calcium, magnesium, zinc, iron or aluminium	First, use complexing agent minimum 2 h after bisphosphonate Second, if not possible: switch to equivalent drug without complexing activity

Part 4: Drug-drug interactions of specific relevance (cont'd)

No	Item	Alternative
76	VKA + vitamin K containing drugs/supplements	First, switch to equivalent drug/supplement without Vitamin K Second, if not possible: monitor INR
77	Any combination of anticholinergic drug	First, replace one of the drugs by an equivalent with less or without anticholinergic activity Second, always advise patients to report anticholinergic side effects

Part 5: General care-related items to be addressed in the community pharmacy

No	Item
78	Dispensation of over-the-counter medication (NSAID, aspirin . . .) was not added in the electronic patient record.
79	Contraindications that can be unambiguously be derived from patient's medication were not added to the electronic patient record
80	Availability of assistance in medication/health issues was not checked nor discussed in frail older patients or older patients with reduced cognition, especially when taking drugs needing strict intake scheme
81	The patient was not asked which aspects of pharmaceutical care could be improved for him/her (translated into practical questions for the specific patient: e.g. correct inhaler use and splitting tablets).
82	Adherence for all chronic medication was not checked or discussed during the past year (refill rate). Adherence for all new medication was not checked or discussed at first refill during the past year?
83	Polypharmacy patients (chronically taking five or more drugs) were not questioned about whether a clear medication scheme was available to him/her

Appendix 4B: GheOP^{3}S criteria that were not applicable to the cohort of patients studied

Part 1a: Potentially inappropriate drugs, independent of diagnosis – drug classes

Criterion number	GheOP^{3}S criterion
3	Any drug for arterial vascular disorders
6	Any long-acting sulfonylurea derivative
7	Any nasal vasoconstrictor ≥ 1 month
10	Any recently marketed drug (black triangles)

Part 1b: Potentially inappropriate drugs, independent of diagnosis – specific molecules

Criterion number	GheOP^{3}S criterion
12	Alizapride
13	Bisacodyl
14	Clonidine
15	Codeine and its derivatives for acute cough
16	Dabigatran
17	Digoxin > 0.125mg/day
19	Ginkgo biloba or Panax ginseng
20	Liquid paraffin
21	Methyldopa
22	Metoclopramide
23	Pentazocine
24	Phenobarbital
25	Pseudoephedrine oral

Part 1b: Potentially inappropriate drugs, independent of diagnosis – specific molecules (cont'd)

Criterion number	GheOP^{3}S criterion
27	Senna glycosides
28	Picosulfate
29	Theophylline
30	Ticlopidine, new prescription
31	Tramadol, new prescription

Part 2a: Potentially inappropriate drugs, dependent on diagnosis – drug classes

Criterion number	GheOP^{3}S criterion
35	Anticholinergics with benign prostatic hypertrophy
38	Oral corticosteroids > 1 week with diabetes
39	Oral corticosteroids > 1 week with hypertension

Part 2b: Potentially inappropriate drugs, dependent on diagnosis – specific molecules

Criterion number	GheOP^{3}S criterion
41	Alizapride with Parkinson's disease
42	Metoclopramide with Parkinson's disease

Part 3: PPOs

Criterion number	GheOP^{3}S criterion
43	The patient is taking an equivalent of 7.5mg of oral prednisone or more for ≥ 3 months and is not prescribed calcium/vitamin D supplementation and bisphosphonates
44	The patient is taking narcotic analgesics and is not prescribed appropriate preventative bowel regimen (preferably macrogol or lactulose)
46	The patient is taking oral corticosteroids for ≥ 1 month and is not prescribed calcium/vitamin D supplementation
48	The patient is taking methotrexate and is not prescribed folic acid supplementation

Part 4: Drug-drug interactions of specific relevance

Criterion number	GheOP^{3}S criterion
49	VKA + oral NSAIDs
51	VKA + antiplatelet drugs, unless prescribed by internist/cardiologist
52	VKA + TMP/SMX
53	Oral NSAID + oral corticosteroids
54	Oral NSAID + diuretic
55	Digoxin + macrolide antibiotics
56	Digoxin + verapamil/diltiazem
57	Lithium + RAAS inhibitors
58	Lithium + oral NSAID
59	Lithium + diuretics
60	Theophylline + quinolones/macrolides

Part 4: Drug-drug interactions of specific relevance (cont'd)

Criterion number	GheOP^{3}S criterion
62	Oral NSAID + selective serotonin reuptake inhibitor/serotonin and noradrenaline reuptake inhibitor
63	RAAS inhibitor + TMP/SMX
66	Alprazolam/midazolam/triazolam/zolpidem/zopiclone + strong CYP3A4 inhibitor
67	Calcium channel blocker + strong CYP3A4 inhibitor
68	Oral NSAID + antiplatelet drugs
69	Phenytoin + TMP/SMX
70	First dose RAAS inhibitor at full dosage + pretreatment with diuretic
71	Tamoxifen + strong CYP2D6 inhibitors
72	Calcium + quinolones/tetracyclines
73	Calcium + strontium ranelate
76	VKA + vitamin K containing drugs/supplements

Part 5: General care-related items to be addressed in the community pharmacy

Criterion number	GheOP^{3}S criterion
79	Contraindications that can be unambiguously be derived from patient's medication were not added to the electronic patient record
80	Availability of assistance in medication/health issues was not checked nor discussed in frail older patients or older patients with reduced cognition, especially when taking drugs needing strict intake scheme

Appendix 5: Results of the pharmacist interventions taken up after 2 months (part 1)

Code	Pharmacist intervention at t = 0	No. of patients	Code	Desired outcome reached at t = 2 months	No. of patients
A1.	Prolonged drug treatment – referral to GP/specialist	6	A2.	Appointment fixed with GP/specialist	3
B1.	Drug prescribed without an evidence-based indication – referral to GP/specialist	2	B2.	Patient took up the referral recommendation and sought medical advice – patient stopped treatment	2
C1.	Consider non-pharmacological approach	2	C2.	Non-pharmacological approach was effective in managing a condition	0
D1.	Referral to GP/specialist depending on underlying condition	1	D2.	Patient took up the referral recommendation and sought medical advice – better management of medical condition	0
E1.	Verify with GP/specialist	0	E2.	Review of any changes in the past 2 months	0
F1.	Check if step-up approach was considered and adopted	0	F2.	Patient took up the referral recommendation and sought medical advice – patient reduced dose	0
G1.	Safer alternative medication available – referral to GP/specialist	1	G2.	Patient took up the referral recommendation and sought medical advice – safer alternative medication was prescribed	0
H1.	Safer alternative medication available – medication switch recommended by pharmacist	2	H2	Patient is satisfied with the safer alternative provided by the pharmacist	1
I1.	Monitoring need	8	I2.	Patient is being monitored	6

Appendix 5: Results of the pharmacist interventions taken up after 2 months (part 2)

Code	Pharmacist intervention at t = 0	No. of patients	Code	Desired outcome reached at t = 2 months	No. of patients
J1.	Start drug at lowest possible dose	0	J2.	Patient took up the referral recommendation and sought medical advice – patient reduced dose	0
K1.	Reduce dose – referral to GP/specialist	3	K2.	Patient took up the referral recommendation and sought medical advice – patient reduced dose	0
L1.	Addition of another drug needed – referral to GP/specialist	0	L2.	Patient took up the referral recommendation and sought medical advice – new drug added	0
M1.	Addition of another drug/vitamins recommended by pharmacist	5	M2.	Patient still takes the other medication/vitamin recommended by the pharmacist	1
N1.	Omission of drug/vitamin recommended by pharmacist	0	N2.	Patient omitted a drug/vitamin as recommended by the pharmacist	0
O1.	Guidance on timing of medications/vitamins	2	O2.	Patient is taking medications/vitamins at the appropriate timings	2
P1.	Patient education	22	P2.	Patient education was maintained	17
Q1.	Discuss with GP/specialist	0	Q2.	Discussion with GP/specialist led to change in pharmaceutical care plan	0
R1.	Influenza vaccine recommendation	24	R2.	Patient took up influenza vaccine	14

Appendix 5: Results of the pharmacist interventions taken up after 2 months (part 3)

Code	Pharmacist intervention at t = 0	No. of patients	Code	Desired outcome reached at t = 2 months	No. of patients
S1.	Recommend assistance in medication/health issues (by nurse, neighbour, relatives etc) in frail older patients or older patients with reduced cognition	0	S2.	Patient acquired assistance in medication/health issues	0
T1.	Aspects of pharmaceutical care that could be improved for the patient were discussed	4	T2.	Change in pharmaceutical care plan was effective for the patient	3
U1.	Adherence for all chronic medication was checked or discussed (e.g. through refill rate) for the past year	77	U2.	Medication adherence was maintained	77
V1.	Polypharmacy patients (chronically taking 5 or more drugs) were provided with a clear medication schedule	9	V2.	Patient is using the clear medication schedule provided	5
W1.	Patient had OTC medication not listed on the patient's electronic record.	21	W2.	Patient's electronic record was updated to include all drugs and vitamins.	19
X1.	Other pharmaceutical intervention not listed above:	1	X2.	Other pharmaceutical intervention not listed above:	1
	Total number of pharmacist interventions carried out	190		Total number of pharmacist interventions that were implemented	151

Appendix 6: Case studies used for the clinical relevance validation (part 1)

The following are real cases encountered during the study. The pharmacist interventions below have been carried out in the community pharmacy after consulting the GheOP³S tool[1]. You are kindly requested to indicate your agreement or otherwise for validation of these pharmacist interventions.

Case 1:

A 69-year old female takes the following medication:

- warfarin (dose according to INR) daily
- amitriptyline 20mg nocte
- bendroflumethiazide 5mg daily
- budesonide 200mcg/dose inhaler 1 puff bd
- ipratropium 20mcg/dose inhaler 2 puffs tds
- lorazepam 1mg daily
- salbutamol inhaler 100mcg/dose 2 puffs prn (max qds)
- valsartan 160mg daily
- paracetamol 1g or paracetamol 500mg/codeine 10mg prn (max qds)

The patient suffers from fibromyalgia, insomnia, asthma, atrial fibrillation and hypertension.

Pharmacist interventions	
Reduction in dose of lorazepam – referral to GP/specialist.	Disagree/ Agree
Patient education on sleep hygiene.	Disagree/ Agree
Patient education on anticholinergic side-effects due to a combination of anticholinergic drugs.	Disagree/ Agree
Influenza vaccine recommendation as the patient does not usually take it.	Disagree/ Agree
Adherence for all chronic medication was checked or discussed (e.g. through refill rate) for the past year.	Disagree/ Agree
Provision of a clear medication schedule.	Disagree/ Agree
Patient did not have OTC medication listed on the patient's electronic record, so such medications were noted on an alternative electronic record available to the pharmacist for follow-up purposes.	Disagree/ Agree

Appendix 6: Case studies used for the clinical relevance validation (part 2)

Case 2:

A 76-year old female takes the following medications:

- amlodipine 5mg daily
- aspirin 75mg daily
- atenolol 100mg daily
- isosorbide mononitrate 60mg daily
- metformin 500mg tds
- perindopril 8mg daily
- simvastatin 40mg nocte
- trimetazidine 20mg tds
- paracetamol 1g prn (max qds)

The patient suffers from ischaemic heart disease, hypertension and type II diabetes. The patient claimed to suffer from constipation sometimes. She said that she has a clear medication schedule available to her.

Pharmacist interventions	
Monitoring need of blood glucose levels.	Disagree/ Agree
Patient education on the use of osmotic laxatives when the patient is constipated (may be linked to the use of amlodipine).	Disagree/ Agree
Patient education on possible changes in awareness of hypoglycaemia (metformin + atenolol may decrease hypoglycaemia awareness).	Disagree/ Agree
Influenza vaccine recommendation as the patient does not usually take it.	Disagree/ Agree
Adherence for all chronic medication was checked or discussed (e.g. through refill rate) for the past year.	Disagree/ Agree
Patient did not have OTC medication listed on the patient's electronic record, so such medications were noted on an alternative electronic record available to the pharmacist for follow-up purposes.	Disagree/ Agree

Appendix 6: Case studies used for the clinical relevance validation (part 3)

Case 3:

A 67-year old female is currently taking the following medications:

- gliclazide 80mg daily prn
- metformin 500mg-1g-500mg daily
- sotalol 80mg bd
- paracetamol prn (max qds)
- Osteocare® 1 daily

The patient suffers from osteoarthritis, type II diabetes and atrial fibrillation.

Pharmacist interventions	
Monitoring need of blood glucose levels.	Disagree/ Agree
Patient education on possible changes in awareness of hypoglycaemia (metformin + sotalol may decrease hypoglycaemia awareness).	Disagree/ Agree
Influenza vaccine recommendation as the patient does not usually take it.	Disagree/ Agree
Adherence for all chronic medication was checked or discussed (e.g. through refill rate) for the past year.	Disagree/ Agree
Patient did not have OTC medication listed on the patient's electronic record, so such medications were noted on an alternative electronic record available to the pharmacist for follow-up purposes.	Disagree/ Agree
Aspects of pharmaceutical care that could be improved for the patient were discussed. It transpired that the patient had a recent increase in the dose of metformin and did not inform the pharmacist of the change and thus she was not being supplied enough metformin. The pharmacist advised her to provide the pharmacy with a prescription for an increase in daily dose of metformin so that her entitlement could be modified.	Disagree/ Agree

1. Tommelein E, Petrovic M, Somers A, Mehuys E, van der Cammen T, Boussery K. Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S) tool. J Public Health (Oxf). 2016;38(2):e158-70.