AGE-RELATED PHARMACOVIGILANCE PERSPECTIVES

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Valerie Lopez Fernandez

Department of Pharmacy

University of Malta

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Dedication

This dissertation is dedicated to Papa God, Mama Mary, Papa Kokoy, Mama Laling, Kuya Mark, baby Am-Am, Didith, Mice and baby Yca.

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ABSTRACT

Drug-related falls are of particular concern in older persons and lead to an increase in morbidity and mortality. Strategies to identify risk of drug-related falls could contribute to optimize patient care.

This aim of the research was to apply pharmacovigilance processes in clinical pharmacy practice within a patient-centric approach and to reduce drug-related falls for older people through medication risk assessment.

The methodology consisted of a four-stage design: (i) A literature scoping exercise to identify fall-risk assessment tools (FRATs); (ii) a pre-intervention study where an identified FRAT was applied retrospectively to evaluate the extent of deprescribing in 55 older patients at a rehabilitation hospital with a history of falls from January to July 2021, using pharmacy patient profiles as a data source; (iii) a presentation of the selected FRAT tool and findings by the researcher to the clinical pharmacists at the rehabilitation hospital so that FRAT was to be used in their daily deprescribing activities; (iv) a post-intervention study starting one month after introducing the selected FRAT tool to the pharmacists, for assessment of the degree of deprescribing in 58 older patients with a history of falls from October 2021 to January 2022. A model for medication risk management for older people was developed.

Literature review (n=88) classified five multifactorial tools and three medication-based tools. The STOPPFall (Seppala et al., 2020) tool from the medication-based category was chosen. From the pre-intervention results, the average age of patients was 81 years (65% females). Hypertension (n=45), diabetes (n=25) and cardiovascular diseases (n=25) were the most prevalent comorbidities. Antidepressants (n=35), diuretics (n=34), opioids (n=31),

and benzodiazepines (n=23) were the most frequent fall risk-increasing drugs (FRIDs) prescribed (N=162). Significant deprescription rates were evident for opioids (97%, $p<0.01$) and benzodiazepines (70%, $p=0.030$). Diuretics (47%), antipsychotics (46%), and antidepressants (37%) showed lower deprescription rates. During the intervention, 9 pharmacists participated who were informed about STOPPFall and encouraged to apply the tool in practice.

The post-intervention resulted in an average age of 79 years (71% females). The most common chronic conditions were cardiovascular diseases (n=40), hypertension (n=40), and diabetes (n=23). Diuretics (n=41), opioids (n=39), and antidepressants (n=26) were the most prescribed FRIDs (N=181). Opioids (97%, $p<0.01$) and antipsychotics (67%, $p=0.027$) were significantly deprescribed. Lower deprescription rates were observed for benzodiazepines (53%), antidepressants (31%), and diuretics (27%). The intervention indicated that the majority of the deprescription rate did not significantly differ when comparing the pre- and post-analyses. A model targeting deprescribing as a pharmacist's pharmacovigilance task in a multidisciplinary approach that must be embedded in a patient-centric system was designed.

This research resulted in the usage of the chosen medication-based fall risk assessment tool within the KGH pharmacy department to assess the range of deprescribing for older patients' high risk of falls and the model was developed as part of the medication risk management.

Keywords: pharmacovigilance, older patients, drug-related problems, falls

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ADE	Adverse Drug Events
ADR	Adverse Drug Reaction
BPH	Benign Prostate Hyperplasia
DBI	Drug Burden Index
DRP	Drug Related Problems
EU	European Union
FRA	Fall Risk Assessment
FRAT	Fall Risk Assessment Tool
FRID	Fall Risk Increasing Drug
JHFRAT	John Hopkins Fall Risk Assessment Tool
MFS	Morse Fall Scale
MRH	Medication Related Harm
PIM	Potentially Inappropriate Prescribing
RR	Relative Risk
STEADI	Stopping Elderly Accidents, Deaths and Injuries
STOPPFall	Screening Tool of Older Persons Prescriptions in Older Adults with high Fall Risk

Chapter 1

Introduction

1.1 Inappropriate Prescribing

Inappropriate prescribing is a preventable risk factor for medication-related harm (MRH) in older persons and can be characterized as drugs that are more likely to harm the individual than to benefit them (Lund et al., 2010; Parekh et al., 2019). Multiple comorbidities and medications, and age-related changes in pharmacokinetics and pharmacodynamics make older patients particularly vulnerable to medication-related harm (Mangoni & Jackson, 2003; Parekh et al., 2019). A recent systematic study of incidence of MRH in older people reports that between 17% and 51% of them acquired MRH within 30 days of discharge from the hospital (Parekh et al., 2018; Parekh et al., 2019). MRH is causing a spike in hospitalisations in England (Veeren & Weiss, 2017; Parekh et al., 2019). The total health expenses of MRH in older individuals after hospital release in England are projected to 477 million euros per year, with hospital returns accounting for 90% of the cost (Parekh et al., 2018; Parekh et al., 2019).

In the United States, over 40% of people above the age of 65 regularly take five or more prescription drugs to discontinue or avoid symptoms and development of the disease (Linsky et al., 2019; Bloomfield et al., 2020). About half of the older patients are taking one or even more potentially inappropriate medications (PIMs). It comprises duplicate drugs and drugs with identified risks or no clear indication (Reeve et al., 2015; Bloomfield et al., 2020). Concurrent multiple treatment is associated with an escalated risk of harmful outcomes such as falls, cognitive weakening and other elderly maladies, hospitalizations and casualty (Scott et al., 2014; Mangin et al., 2018; Bloomfield et al., 2020).

Prescribing potentially inappropriate medications (PIMs) to older persons has been a prominent issue for several decades, and a major public health concern, with estimates ranging from 5.2% to more than 85% of older people being prone to receiving PIMs (Bala et al., 2018; Chen et al., 2019). Poor prescribing quality which is frequently associated to multiple drug treatments is projected to have resulted in the administration of inappropriate drugs to 50% of the older people (Fialova et al., 2005; Marengoni et al., 2015). Modifiable variables such as drug-drug interactions comorbidities, and multiple drug treatments most likely increase adverse drug reactions (ADRs) and account for 5% to 10% of hospital costs which linked to span of stay, illnesses, and death (Budnitz et al., 2011; Marengoni et al., 2015).

1.2 Drug-Related Problems

Drug-related problems (DRPs) are occurrences or situations concerning prescribed medication that actually or possibly impede with the intended health outcomes. These issues can appear as disparity, errors, poor compliance, multiple drug therapy, adverse drug events (ADEs), and other drug-related complications. They are a complex situation that can arise in numerous repeat admission once they happen in the aging population during the care coordination from admission to discharge (Coleman et al., 2006; Quinalha & Correr, 2010; Valente et al., 2019). The older population are generally recipients of care from a variety of health care experts and regularly moves in various medical services, making them vulnerable to alterations in medication treatment and care shortfalls during transfer of health keeping management (Trompeter et al., 2014; Valente et al., 2019). DRPs or harmful implications due to drugs are responsible for 30% of aged people hospital admissions on

average. Agreement among experts that 50% to 70% of these difficulties are preventable (Quinalha & Correr, 2010; Valente et al., 2019).

Drug-related problems can pose a huge public health challenge around the world. A previous study by Budnitz et al. (2006) as cited in Silva et al. (2015) revealed that on national surveillance of emergency department visits for outpatient adverse drug events, cited by Silva et al. (2015), DRP is the 4th-6th chief cause of death in the United States, and adverse reactions account for 3-6% of admittance (700,000 patients per year) at a cost of $130 billion dollars. Maher et al. (2014) and Placido et al. (2020) also affirmed that drug-related problems that DRPs are the underlying cause of an elevated risk of hospital admissions and emergency department visits. According to Perez et al. (2018) and Placido et al. (2020), older people are predisposed to taking numerous medicines and metabolize drugs differently than younger individuals which may contribute to escalate DRPs and also drug-related hospital admissions. Some of the factors that cause of drug-related problems and the need for emergency hospital contacts consist of a lack of regularity in physician communications, a shortage of a constant list of drugs, and insufficient prescribing and supervising of therapeutic plan (Hajjar et al., 2007; Milos et al., 2013).

1.3 Death Due to Falls

In 2015, the European Association for Injury Prevention and Safety Promotion (EuroSafe) stated an estimation of 35,848 older people (65 and older) resulted in death due to falls in the European Union (EU) each year (data 2010-2012)[1]. The number mentioned is a

[1] European Public Health Association. Falls among older adults in the EU-28: Key facts from the available statistics [Internet] EUPHA; 2015 [cited 2022 Apr 11]. Available: https//eupha.org/repository/sections/ipsp/Factsheet falls in older adults in EU.pdf

projected underestimation of the actual figure of fall-related deaths. Among the 35,848 older adults fall-related deaths, 88% are people aged 75 years and above, whilst 59% are women. Along with this data, 28 deaths were reported among 526, 893 patients in Malta, with an incidence rate (IR) of 5.38 deaths per 100,000. Based on a survey of more than 200 hospitals from all over Europe, it is approximated that 3.8 million older adults visit emergency departments (ED) each year within the EU for a fall-related injury, with 1.4 million hospitalised for more rehabilitation. If no supplemental fall prevention strategies are implemented, the yearly number of fall-related ED visits is predicted to exceed six million by 2050, with 2.3 million cases or more seeking treatment and requiring long-term medical care[1].

1.4 Drug-Related Falls

Each year, roughly 2.3 million individuals in the EU[2] and 2.8 million in the US[3] are admitted to hospitals with fall-related injuries with 36,000 adults in the EU and 27,000 older people in the US died as a result of their injuries. The cost of health care fall-related injuries approximated to be 25 billion euros in the EU[4]. Numerous older individuals are worried of falling, which can lead to psychological problems such as mental stress, depressed mood or anxiousness. Various reviews that include systematic reviews and meta-analyses have identified psychotropic drug consumption as an independent risk factor for falls. Nonetheless, most earlier research findings on psychotropic drug usage and falls

[2] Key facts from the available statistics: EuroSafe, Amsterdam 2015. Falls among older adults in the EU-28 [Internet]. Amsterdam: EUPHA; 2015 [cited 2022 Mar 15]. Available: https://eupha.org/repository/sections/ipsp/Factsheet_falls_in_older adults_in_EU.pdf.
[3] Centers for Disease Control and Prevention. Falls and fall injuries among adults aged ≥65 years-United States, 2014 [Internet]. United States: CDC; 2016 [cited 2022 Mar 15]. Available: https//www.cdc.gov/mmwr/volumes/65/wr/mm6537a2.htma
[4] Key facts from the available statistics: Eurosafe. Amsterdam 2015. Falls among older adults in the EU-28 [Internet]. Amsterdam: EUPHA; 2015 [cited 2022 Mar 15]. Available: https://eupha.org/repository/sections/ipsp/Factsheet_falls_in_older adults_in_EU.pdf

focused on only a subset of the significant health conditions attributed with falls such as impaired vision, debilitation, polypharmacy, functional limitations and use of drugs that enhances fall risk (Du et al., 2017).

According to Centers for Disease Control and Prevention, falls among seniors 65 years and older caused the death of over 34,000 people in 2019 making it the highest incidence of injury-related mortality in that age group[5]. In the United Kingdom alone, patient falls in medical care facilities cost approximately 92 million pounds per year[6]. Nearly one-third of older people over 65 years staying in long-term health care accommodations fall annually which leads to bone fractures, diminished quality of life, compromised independence, anxiety of falling, impairment, and premature death (Ambrose et al., 2015; Bor et al., 2017). Medication consumption is also an important extrinsic risk factor for falls. Even though chronic conditions in elderly individuals frequently necessitate the use of multiple prescription medications, they were revealed to be an independent risk factor for falls (Weber et al., 2008; Wu et al., 2013; Bor et al., 2017). Potentially inappropriate medication (PIM) lists have been performed to help lower the risk of falls and the prevalence of adverse drug events with the 'Beers criteria' being the most commonly utilised (Beers et al., 1991; Bor et al., 2017).

Andersen et al. (2020) discovered that the most common cause of falls among 82 older patients aged 65 years and up admitted to Danish University Hospital was the use of

[5] Centers for Disease Control and Prevention. Older Adult Fall Prevention [Internet]. United States: CDC; 2021 [cited 2022 Mar 09]. Available: http://www.cdc.gov/falls/

[6] The National Patient Safety Agency (NPSA). The third report from the Patient Safety Observatory Slips, trips and falls in hospital [Internet]. London: NPSA; 2007 [2022 Mar 10]. Available: http://www.mtpinnacle.com/pdfs/slips-trips-fall-2007.pdf

medicines with dizziness as recognised side effect [n=21 (10.5%)], followed by the usage of blood pressure-lowering drugs [n=17 (8.5%)] as these patients had orthostatic hypotension symptoms. There was functional impairment in 12 patients (6%) and accidental occurring by impacting balance or cognition in 11 patients (5.5%), both of which resulted in a fall due to medications. In addition, 141 patients were identified to be taking potentially inappropriate medications (70.5%). It was noticed that PIMs were determined in 79 (96%) patients who were regarded to have a suspected drug-related fall as compared to 62 (52%) of 118 patients without utilising it.

Findings reveal links between certain prescription drugs and the risk of falling. Blood pressure-lowering agents, some pain relievers, antidepressants, anxiolytics, and sedative hypnotics were all identified as fall risk factors (Ebly et al., 1997; Smith, 2003; French, 2006). A meta-analysis of 40 reviews on psychotropic drugs (such as benzodiazepines, hypnotics, neuropleptics, analgesics, and hypnotics) observed a connection between drug use and falls (Leipzig et al., 1999; French, 2006). Additional 29 meta-analysis studies on analgesic and cardiac medications encountered an elevated risk of falling. Finally, administering of more than four drug treatments or some psychoactive drugs raised the potential of falling (Leipzig et al., 1999; Smith, 2003; French 2006).

1.4.1 Fall Risk-increasing Drugs

Falls are the prominent source of injury for older individuals in the general population and also with the ones suffering from intellectual disability. Enumerated risk factors for falls comprise a number of drugs that are presumed to be fall risk-increasing drugs (FRIDs). In a

this Swedish national registered-based study, persons with an intellectual disability seem to have received more prescriptions for at least one FRID (Relative Risk [RR] 2.31). Antipsychotics encountered the greatest increase (RR 25.0), accompanied by anxiolytics (RR 4.18), antidepressants (RR 2.72), and hypnotics and sedatives (RR1.42). Opioids were observed to have a lower prevalence (RR 0.74). Those who had at least one FRID prescribed drug were far more likely to experience a fall-related injury that necessitated medical attention in both cohorts. The elevated risk was greater in the referent cohort (RR 3.98) than in the intellectual disability cohort (RR 2.27), but people with intellectual disability and medication seemed to have a greater risk of falling than those with prescription in the referent cohort (RR 1.27). A close trend was noticed for all drug classes, excluding opioids, where prescription performed the same chances of acquiring a fall-related injury that entailed medical attention in both cohorts (Axmon et al., 2018).

Zia et al. (2016) found that utilisation of multiple FRID is responsible for the correlation between polypharmacy and falls in the aging population. The rising number of treatments, also referred as "polypharmacy," carries the potential of FRID use which increases the likelihood of falls, whilst polypharmacy without the availability of FRID may not be attributed with falls, therefore the term "polypharmacy" may not be applicable to fallers. This is supported by the result which revealed that the correlation of polypharmacy with falls was weakened but having two or more FRID continued as an independent factor for falls. The use of single FRID was not attributed with falls but $\geq$2FRID were significantly correlated with falls. When participants taking $\geq$ 2FRID were removed, the occurrence of polypharmacy was not related with falls among the rest of the participants. Once

participants into polypharmacy were removed, the use of ≥ 2FRID was significantly remained to be associated with falls.

Low et al. (2019) investigated the consumption of FRIDs in patients aged 65 years and older (n=124) in a tertiary teaching hospital in Malaysia, the majority of whom had fall-related fractures (83.1%) and hip fractures (67%). The older adults or those over the age of 80 had a significantly higher rate of hip fractures than younger people (p=0.009). Approximately 75% of this patient group that suffered fall-related fractures had taken at least one FRID prior to admission. When compared to the elderly, younger people used significantly more FRIDs, notably blood pressure-lowering agents (p=0.017). The huge proportion of them (>80%) were still receiving FRIDs during hospital discharge and deprescribing was initiated in less than a quarter of this patient group. Moreover, 32.6% of them seem to have either new FRIDs added or FRID doses increased at the time of hospital released.

1.5 Fall Risk Assessment Tools

The climbing event of falls in geriatric rehabilitation institutions may be clarified by the real sense that older adults are commonly fragile and are more vulnerable to risk factors and chances of falling than younger sick people. They are motivated to be physically operational, unconstrained, and engaged in treatment programs in rehabilitation settings (Saverino et al., 2006; Vieira et al., 2011; da Costa et al., 2012). These scenarios put their physical capabilities to test and situate them in cases where they are more prone to fall (Saverino et al., 2006; da Costa et al., 2012). Whilst there is a definite requirement for

approaches to avert elderly inpatient falls in rehabilitation facilities, it is ambiguous which schemes are by far the most efficient in avoiding fall in these residents (Gillespie et al., 2003; da Costa et. al., 2012). In 2007, Patient Safety Observatory reported the use of fall risk prediction tools is an established strategic approach (da Costa et al., 2012). Classifying fall-prone patients at the beginning of hospital admittance may support in the prevention of falls by leading the application of specific fall prevention methods. However, the validity of the available screening tools in recognising fall-prone patients is still subject to arguments (Morse, 2006; Oliver, 2006; da Costa et al., 2012). Imprecise falls screening tools may instil a false feeling of security for both patients and health care team, placing patients susceptible to the possible detrimental consequences of falling resulting to injuries (Oliver, 2006; da Costa et al., 2012).

Several screening tools have been created to detect fall risk in older persons. A recent meta-analysis recognised 26 fall risk assessment tools presently used for sensing older adults prone for fall risk which include Hendrich II Fall Risk Model, STRATIFY, Morse Fall Scale (MFS) and John Hopkins fall risk assessment tool, among others (Park, 2018; Glass et al., 2020). These tools typically consist of a scoring mechanism designed to gauge the cumulative result of establish risk factors to distinguish those patients who are most vulnerable to falls (Carpenter et al., 2014; Glass et al., 2020). No consensus has been acknowledged so far on the ideal evaluation clinical tool. It appears that the current fall risk assessment tools for the older adults do not reliably determine elderly fallers (Park, 2018; Glass et al., 2020). The majority of fall risk assessment (FRA) currently applied tend to involve intrinsic risk factors comprise origin of falling, health problems (e.g., orthostatic

hypotension, urinary incontinence), complex medication usage (e.g., polypharmacy), medical device use (e.g., walking stick, walker aid), and gait concerns. Extrinsic factors (e.g., surroundings that designates slip hazard) are generally acknowledged by amenity maintenance operations and building design (Dykes, 2017; Norman & Hirdes, 2020).

1.5.1 Medication-related Fall Risk Assessment Tools

Recent research of Michalcova et al. (2020) has shown that various fall risk assessment tools that have been produced do not consist of drug as a risk factor. An evaluation of 20 fall risk assessment tools discovered that only seven of them take medication use into account as a potential cause (Perrel et al., 2001; Michalcova et al., 2020). Medication utilisation in a fall risk assessment is now incorporated in more latest tools, such as The Johns Hopkins Fall Risk Assessment Tool, which ranks opiates, hypnotics, anticonvulsants, sedatives, diuretics, antihypertensives, laxatives, and psychotropics as increase fall risk medications (Poe et al., 2007; Michalcova et al., 2020). The Johns Hopkins Fall Risk Assessment Tool is well-organized and validated, but there are a lot of risk points to evaluate which is maximum of 28. This renders analysing the fall risk more time laborious for medical care practitioners than using a tool with lesser risk points, like the five items proposed for usage in our latest upgraded fall risk assessment tool. The tool is distinctive that the fall risk drug listed was created by means of statutory drug information available in product characteristics summaries authorised by EU (Michalcova et al., 2020). According to Seppala et al. (2020), because emerging lists do not reflect a comprehensive and homogenous drug list to avoid in older people at risk of falling, a tool for deprescribing targeting solely on drug-related falls may be more effective in avoiding falls than a usual

prescribing tool. To have the opportunity to thrive, such a tool should be embedded in a multifactorial falls preventative measures.

Fall prevention multifactorial tool have been manifested to minimize both the rate and risk of falls commonly comprise a drug review and modification element (Hopewell et al., 2018; Blalock et al., 2020). Only three studies have been published that investigated the usefulness and efficiency of community-based, single-factor fall prevention measures that pivoted on drug review and modification (Blalock et al., 2010; Mott et al., 2016; Boye et al., 2017; Blalock et al., 2020). Noticeably, these studies applied different qualifying standards: a fall within a 12-month period regardless of medication use (Mott et al., 2016; Blalock et al., 2020); utilisation of more than four drugs with Central Nervous System mechanism (Blalock et al., 2010; Blalock et al., 2020); at least one FRID in the regimen where FRIDs consisted cardiovascular agents and other drugs in which lacking coherent evidence that they substantially augment fall risk. In this research, an investigation whether Drug Burden Index (DBI) might deliver a tool that can be used to classify people at high risk of medication-related falls throughout upcoming intervention studies (Blalock et al., 2020). The DBI is a validated measure for analysing a person's total access to treatment with sedative and anticholinergic mechanisms comprising also of those medications associated to enhance the risk of fall (Hilmer et al., 2007; Blalock et al., 2020). Previous studies have revealed that DBI can forecast falls and other outcome measures in older adults. It has a potential to be employed in clinical environment to determine high risk for medication-related falls in older people (Kouladjian, 2019; Blalock et al., 2020).

1.6 Pharmacovigilance Role of Clinical Pharmacists

The function of the clinical pharmacist being part of the health care professional team plays a pivotal position in maximising medication therapy in the vastly growing population of older patients (Schmidt et al., 1998; Verrue et al., 2009; Spinewine et al., 2012; Gauci et al., 2018). A pharmacist's intervention documentation provides a record that is relevant for the continuous flow of care, operation of pharmacist services, and quality assurance (American Society of Health-System Pharmacists, 2003; Royal Pharmaceutical Society, 2006; Gauci et al., 2018). Maldonaldo et al., (2014) further discussed that as compared to outpatients, hospitalized older patients are typically more unwell. Engaging active pharmacovigilance operations among older individuals allows health care providers to detect medication-related problems in a facility where assessments can be made immediately after incorrect prescribing and whose output is traceable, and thus more quickly rectified.

Pharmacists in long-term care institution can be in the best stance to deliver fall risk mitigation management by undertaking definitive and ongoing resident therapeutic plan assessments addressing fall risk (Becker & Rapp, 2010; Boyle et al., 2010; Rojas-Fernandez et al., 2014). This is not a trivial matter because if pharmacists do not take an active role in these concerns during medication utilisation reviews, significant possibilities for enhancing therapeutic regimen reviews may be neglected. It has been revealed that no available pharmacy report succeeded in the fall that targets prospectively configurable drug-related risk factors in hospitals among 103 residents of retirement villages in Ontario, Canada who encounter >1 fall in one year. Indeed, pharmacists acknowledged that taking

into account, falls is not a usual practice in their medication reviews (Rojas-Fernandez et al., 2012; Rojas-Fernandez et al., 2014). A practical figuring from the pharmacists recommended that if probable, a concise algorithm or flow chart for addressing falls could even facilitate them in establishing potentially modifiable risk factors for falls which could then be tackled with the doctor (Rojas-Fernandez et al., 2014). Several tools are available to measure patients at risk of fall but there seems to be no user-friendly systematic means of detecting and mitigating fall risk that pharmacists could use in executing their routine tasks (Bergman-Evans, 2006; Cooper & Burfield, 2009; Rojas-Fernandez et al., 2014). Others have designed complicated clinical practice algorithms that are underutilized (Quigley, 2007; Bulat et al., 2008a; Bulat et al., 2008b; Bulat et al., 2008c; Rojas-Fernandez et al., 2014). Thereby, a demand for clinical-based tool that is logically simple and unambiguous must be integrated into pharmacists' daily functions (Rojas-Fernandez et al., 2014).

A 2013 Cochrane review resulted in a 36% decline in emergency unit fall cases from a month to a year after hospital release due to inpatient medication utilisation review performed by doctors, pharmacists and other practitioners of the health care team (Christensen & Lundh, 2013; Lai, 2017). A subside in deaths and referrals to emergency care, lessening of tremors and incapacity and an improvement in vigilance were observed in a nonrandomized controlled trial in nursing care settings that used an algorithm to trace inappropriate prescribing (Garfinkel et al., 2007; Lai, 2017). A follow-up study using this similar algorithm in community-residing patients demonstrate a reduction of 88% when multiple drug therapy was well managed (Garfinkel & Mangin, 2015; Lai, 2017). Proper stoppage of statin drugs to patients with less than a year to live responded with a better

quality of life with a drop in drug cost (Kutner et al., 2015; Lai, 2017). Karani et al. (2016) discussed that pharmacists can screen for fall risk using clinical tools, assess and modify drug therapy, and help educate patients and caregivers how to prevent falls. The tools are being improved to increase pharmacists' engagement in reviewing medications, classifying those that lead to an increased risk of falling and conveying those concerns to patients' primary care doctors.

1.7 Deprescribing

Almost half of all older adults consume more than five medications and one in every five of these prescribed drugs is most likely inappropriate[7]. Older people who are given a greater number of medications has a greater tendency to be hospitalized due to adverse drug reaction[8]. Whilst any medication has the characteristics of being beneficial, it also has the potential to cause harm. When taken together, the threats of drug interactions as well as the accumulated harm can surpass the benefits. This implies that clinicians must possess a vital skill for prioritizing ongoing therapy. Deprescribing is one aspect of good prescribing, which is the approach of calibrating drugs to its lowest effective therapeutic dose or discontinuing it when the regimen dangers the patient's health condition rather than benefitting from it (Farrel & Mangin, 2019). Patients prefer to take lesser medications but frequently depend on clinicians to initiate the conversation (Reeve et al., 2013; Farrel & Mangin, 2019). The discussion should be centred on assisting patients in comprehending that minimizing or withdrawing medications upholds the quality of life to its best whilst

[7]Centers for Disease Control and Prevention. Health, United States, 2016 With Chartbook on Long-term Trends in Health-United States, 2016 [Internet]. United States: CDC; 2016 [cited 2022 June 02]. Available: https//www.cdc.gov/nchs/data/hus/hus16.pdf
[8] Canadian Institute for Health Information. Drug Use Among Seniors in Canada, 2016-Canada, 2016 [Internet].Canada:CIHI;2016 [cited 2022 June02].Available: https://secure.cihi.ca/free_products/drug-use-among-seniors-2016-en-web.pdf

optimising the advantages of the therapy where there is compelling evidence for ongoing benefit in this age cohort (Farrel & Mangin, 2019).

Deprescribing is an intricate and multifactorial process with various methods. There are recommendations and tools currently offered on a global scale to guide clinicians and patients in determining and discontinuing safely inappropriate medications following a shared decision-making drugs optimisation evaluation. The rising allocation of treatment options and utilisation of single disease model standards have resulted in a healthcare structure that is tailored towards prescribing, with deprescribing frequently shown as a completely independent operation. Deprescribing should indeed be viewed as a part of prescribing and is a pertinent factor in making sure that patients still receive appropriate prescribed drugs with right doses for them (Le et al., 2019).

A study was performed by Marvin et al. (2016) which aimed to quantify the problem and determine whether drug review in Chelsea and Westminster Hospital resulted in the deprescribing of medications associated with a higher risk of falling. It was revealed that the pharmacists conducted a drug review (with or without changes) involving 45/86 (52%) cases. In these 45 patients, the number of fall risk-increasing drugs reduced by a mean of 0.53 before and after assessment (not including dose reductions). It is worth considering that a pharmacist was behind, and changes were recorded for each case where a drug review contributed to a decrease in fall-risk drugs for patients.

1.8 Aims and Objectives

The study explored the application of pharmacovigilance processes in clinical pharmacy practice within a patient-centric approach for older patients. It specifically sought to:

1. review medication risk assessment tools specific for older patients;

2. review and compare fall risk assessment tools for clinical pharmacy practice;

3. assess the extent of deprescribing to prevent falls in a cohort of older patients.

Chapter 2

Methodology

This chapter describes the flow of the methodology used in the study to examine the utilisation of pharmacovigilance processes in reducing drug-related falls among older people in a clinical pharmacy practice setting at Karin Grech Hospital (KGH). It contains the research setting, research design, and procedures necessary for the completion of the study.

2.1 Research Setting

The study was conducted in Karin Grech Hospital (KGH), a 280-bed hospital specialising in the rehabilitation of older patients situated in Pieta, Malta. KGH is actively delivering quality services to all admitted patients during their hospital stay. The Pharmaceutical Services at KGH provide the patients with an easy-to-follow therapeutic plan to encourage adherence and enhance safety in drug administration after discharge.

2.2 Research Design

The study followed a qualitative research design which consists of four stages (Figure 2.1), (**i) identification of tool for medication-related falls:** literature search of relevant studies was utilised in selecting the most appropriate tool among persons 60 and older with a history of fall, **(ii) pre-intervention study:** pharmacy patient profiles were analysed to assess the extent of medication review conducted to decrease the risk for falls, **(iii) intervention by the researcher:** the researcher presented the selected fall risk assessment tool to the clinical pharmacist at the hospital for use in daily practice, **(iv) post-intervention study:** after a one-month period, the researcher analysed the pharmacy patient profiles of discharged patients to evaluate the degree of deprescribing implemented after using the chosen clinical tool.

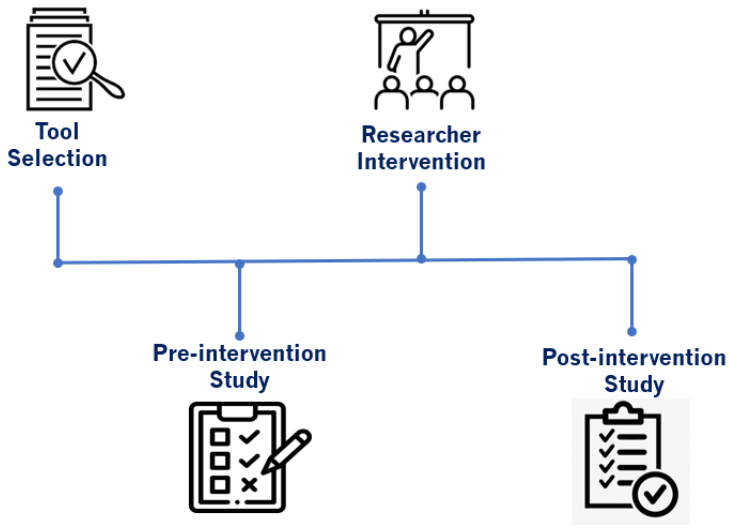

Figure 2.1 Flowchart of the Study Design

2.3 Literature Evaluation

A literature search was performed to assess a validated medication-related studies. Literature was identified from peer-reviewed journals and research papers through an electronic search of Medline/PubMed, Hydi, Proquest Central and Google Scholar published from 2010 to 2021. The search terms used in this review were medication or drug-related or based fall risk assessment tool, fall risk assessment or validated or screening tools, fall risk increasing drugs, geriatrics or elderly and older adults or older people. Inclusion and exclusion criteria for the review were depicted in Table 2.1 to guide the selection of the clinical assessment tool to be utilised in the study. The order in retrieving articles and relevant studies is also shown in Figure 2.2.

Table 2.1 Inclusion and Exclusion Criteria for Literature Evaluation

Criteria	Description
Setting	*Include*: Hospitals (public and private); home care; rehabilitation; residential aged care; community dwelling; nursing homes; *Exclude*: Ambulatory hospitals; clinics
Age	*Include:* ≥ 60 year old Exclude: ≤ 60 year old
Intervention	*Include*: Evaluation of medication-related fall risk assessment studies; evaluation of multifactorial fall risk assessment tools that include medication or drug content category; other strategies of assessing medication-related studies which includes clinical judgement *Exclude*: Evaluation of non-medication-related fall risk assessment studies; evaluation of multifactorial fall risk assessment tools that do not include medication or drug category
Outcome	Prediction of falls may include one of the following: • Prospective validation in > 1 population • Sensitivity and specificity analyses • Validity • Reliability • Simple calculation of score Medication-related or drug-related
Publication details	*Inclusion:* Systematic reviews, meta-analysis; prospective studies and reviews about multifactorial fall risk assessment tools (with medication or drug-related category) and medication-related fall risk assessment tools studies; reviews or studies focusing on medication-related in assessing fall risk *Exclusion*: Reviews or studies evaluating fall risk assessment tools with no medication or drug category
Limitation	2010-2021; Published in English; Humans
Databases	Medline/PubMed, Hydi, Proquest Central and Google Scholar

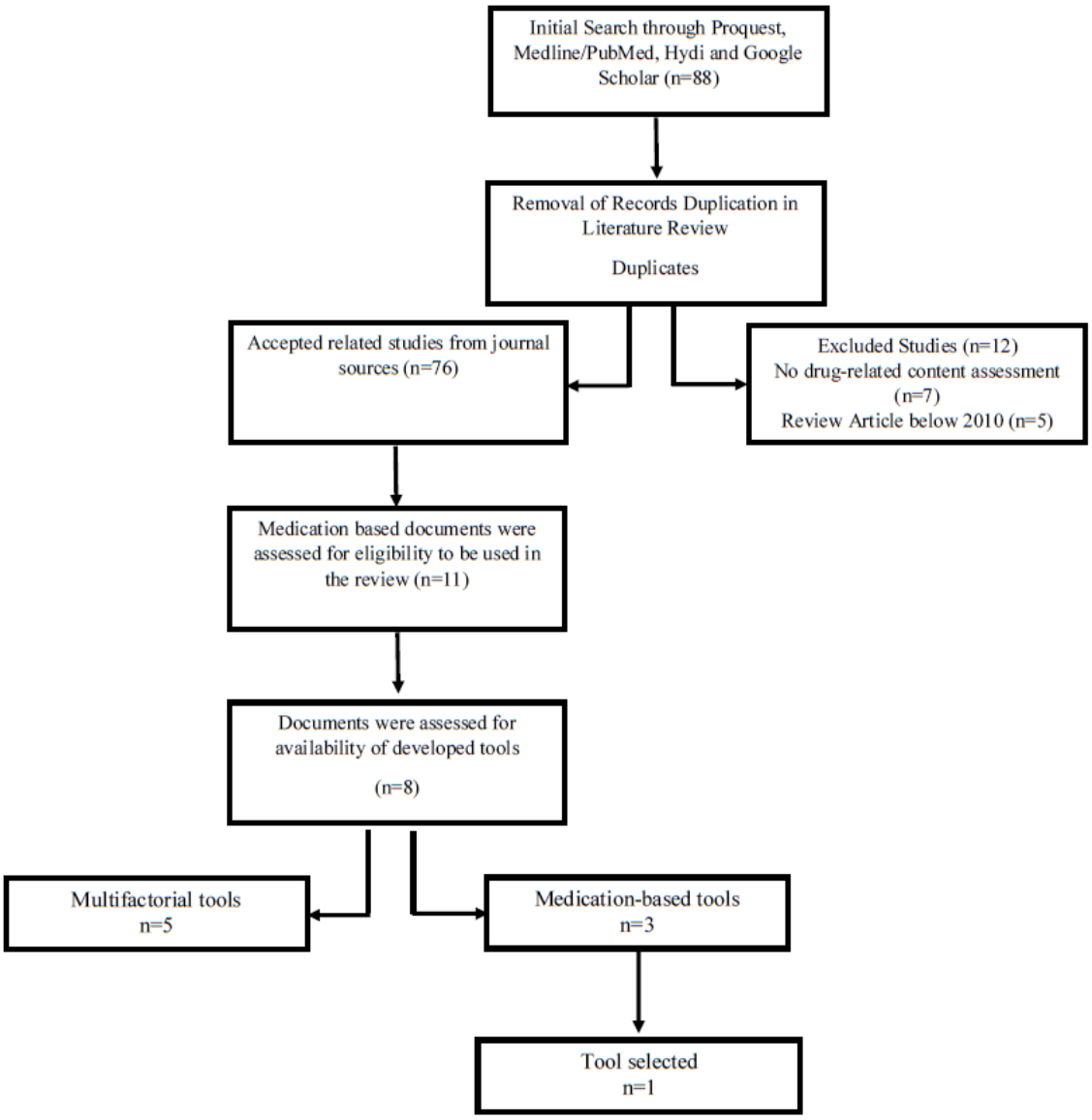

Figure 2.2 Diagram in Selecting Medication-based Tool

2.4 Comparative Analysis of Fall Risk Assessment Tools

The identified eight fall risk assessment tools underwent a critical assessment process in order to determine which among the clinical tools is best and appropriate for use in the setting. The medication-based fall risk assessment tool was chosen and categorized after a

thorough assessment of its components in terms of type of tool-intervention used, presence of reliability and validity test, and statistical interventions employed and its results (refer to Appendix 2). Validity, reproducibility, equivalence, feasibility, and acceptability were the principles used in assessing the tools as identified by Norcini et al. (2011). Table 2.2 describes the characteristics and features of each criterion. All the identified fall risk assessment tools were scrutinized and given one point if successfully achieved the standards outlined in the description.

Table 2.2 Criteria for Good Assessment

Criteria	Description	Points
Validity	If the assessment tool indicated procedure of review by experts. Having presented assessors' findings of the tool and statement that recommendations were considered, and the tool was revised accordingly.	1
Reproducibility	Internal validation was undertaken with at least a Cronbach's alpha analysis of more than 0.7. The study should also indicate performance of sensitivity and specificity analyses, odds ratio or risk ratio analysis and or conducted a Receiver Operating Characteristic analysis showing the strength of the tool in terms of Area Under Curve.	1
Equivalence	There should be at least an analysis comparing its performance against a more standardized test of a higher caliber and or comparative analysis versus a commonly used similar assessment tool.	1
Feasibility	Given the requirements of the design of the study at hand the availability of data during data collection, the assessment tool may be performed with ease. The instrument must be medication-related focus and the use of fall risk-increasing drugs (FRIDs) among older adults.	1
Acceptability	Acceptability of the tool means that the tool has not only been studied but applied in a larger target population and or have been tested to different contrasting environments.	1

2.5 Pre-intervention Study

To assess the extent of deprescribing performed to reduce the risk of falls, the pharmacy patient profiles were reviewed retrospectively to identify patients admitted with falls. Patients aged 60 and up who were hospitalized to KGH with a history of fall with or without a fracture and discharged between January and July 2021 met the inclusion criteria. Deceased patients, patients discharged to acute care, patients under the age of 60, and those diagnosed with a mechanical fall were all excluded. The prescribed medications listed in each pharmacy patient profile were examined and classified according to the 12 drug class lists *(benzodiazepines, antidepressants, antipsychotics, opioids, antiepileptics, diuretics, centrally-acting antihypertensives, cardiac vasodilators, alpha-blocker antihypertensives, alpha-blocker for Benign Prostate Hyperplasia (BPH), sedative antihistamines, and drugs for overactive bladder and urge incontinence)* as FRIDs enumerated by the selected tool, the Screening Tool of Older Persons Prescriptions in older adults with high fall risk (STOPPFall). Deprescribing was measured if the medication's dose of a particular FRID from the first day of admission up to the treatment discharge list was reduced or stopped. Reduced means the drug's dose was decreased and included as one of the discharged medications. A reduced drug is always a take-home medication with decreased dose. Stopped means the drug's dose was maintained, increased or decreased during the entire admission but not incorporated in the treatment discharge list. A stopped drug is always not considered a take home medication. Non-deprescribing was evaluated if the dose of the prescribed drugs were maintained and increased but definitely not decreased as a discharged medication. A non-deprescribed drug always ended up as a discharged or take-home medicine. It was further assessed as documented or not documented. Documented

means that a non-deprescribed drug was mentioned in the active problem section of the patient profile or reason was stated for its prescribing. It is also discussed in pharmaceutical care issues as one of the agents to be monitored due to risks, side effects, and other concerns. Not documented is when no trace of information of a non-deprescribed drug discussed either in active problems or pharmaceutical issues section.

2.6 Intervention by the Researcher

The researcher presented the chosen fall risk-assessment tool (STOPPFall) to the clinical pharmacists at KGH during the Falls Prevention Week in September 2021 through a formal presentation which was followed by discussion. The history and creation of the clinical tool which included the governing bodies and panellists who participated in its development, and the vigorous consensus of producing the identified FRIDs list were tackled. The variation in fall-risk in relation to sedative effects, potential to induce orthostatic hypotension and anticholinergic activity within pharmacological subclasses were explained. The retrospective analysis findings of the pre-intervention study regarding the extent of deprescribing and care issue documentation were presented. A discussion was held with a focus on drugs which were shown not to be deprescribed and care issues not documented in the pre-intervention study. Instructions on the application of the electronic tool and its components including when to take into account deprescribing STOPPFall medications, and how to monitor patients' clinical status after deprescribing were also provided. the clinical pharmacists were encouraged to use the chosen tool in daily clinical practice.

2.7 Post-intervention Study

The researcher started to examine the pharmacy patient profiles one month after the tool was presented. The assessment employed the same procedures, inclusion, and exclusion criteria as in the pre-intervention stage. The profiles selected were those of patients discharged between October 2021 to January 2022. The prescribed drugs for each profile were identified and categorized using the STOPPFall listed FRIDs. Deprescribing was determined if the drug's dose was reduced or stopped, whilst non-deprescribing was determined by whether or not the medication was documented. The procedure of analysis adopted was the same as for the pre-intervention study so that the data could be compared.

Chapter 3

Results

This chapter describes the data and results gathered from literature review and pre and post-intervention assessments.

3.1 Tools Identification

In the search, 88 research articles were retrieved from various databases and websites. A total of 76 relevant studies from journal sources were accepted after a literature scoping exercise. Twelve studies were omitted, seven of which did not include medication evaluations and five were published before 2010. Eleven medication-based studies satisfied the criteria for inclusion and were considered for further evaluation. Eight of these resulted in the development of a tool, five of which were multifactorial studies consisting of two research reviews, two reports (one evidence-based and one Centers for Disease Control recommendation), and one meta-analysis review. Multifactorial tool is an assessment that contains components such as gait, balance, mobility and medicine etc. to determine a person's risk of falling. Six medication or drug-based studies were grouped, 3 of which generated a tool or system for medication review with each has its own research design such as delphi process, retrospective cohort and validation and evaluation phase design. The remaining 3 studies were eliminated because no tool was established. The final tool was selected from this category. Table 3.1 shows the identified medication-based fall risk assessment studies.

Table 3.1 Medication-based Falls Risk Assessment Articles

Description	Abbreviation	References (Author & Year)
Multifactorial Studies		
1. The Downton Fall Risk Index	Downton	Da Costa et al., 2012
2. Fall Risk Assessment Tool	FRAT	Welch et al., 2016
3. Stopping Elderly Accidents, Deaths and Injuries	STEADI	Lohman et al., 2017
4. John Hopkins Fall Risk Assessment Tool	JHFRAT	Poe et al., 2018
5. Hendrich II Fall Risk Model	Hendrich II FRM	Hendrich et al., 2020
Medication-based Studies with Tool or System Produced		
6. The Drug Burden Index Calculator	DBI Calculator	Kouladijan et al., 2016
7. Drug Burden Index	DBI	Blalock et al., 2018
8. Screening Tool of Older Persons Prescription in older adults with a high fall risk	STOPPFall	Seppala et al., 2020
Medication-based Studies without Tool or System Produced		
9. Development of a Risk Assessment Tool for Falls Prevention in Hospital Inpatients Based on Medication Appropriateness (MAI) and Modified Beer's Criteria		Rumore et al., 2012
10. Effectiveness of medication withdrawal in older fallers: results from the Improving Medication Prescribing to reduce Risk of Falls (IMPROveFALL) trial	IMPROveFALL	Boyé et al., 2017
11. Inclusion of medication-related fall risk assessment tool in geriatric care units		Michalcova et al., 2020

3.2 Comparative Result of Fall Risk Assessment Tools

The STOPPFall Fall Risk Assessment Tool got the highest score as revealed in Table 3.2 among the other fall risk assessment tools identified. Each tool was validated by experts, either through the Delphi method or the usual review of identified experts in the field. Internal reliability tests and diagnostic performance evaluation results were provided by every tool. Equivalence testing was performed on STEADI, Hendrich II, STOPPFall, DBI and DBI Calculator whilst none was seen in JHFRAT, FRAT and Downton. Feasibility was also tested where a chart review of patients able to yield information that the tool can directly utilized, and only JHFRAT and STOPPFall generated analyses directly from the used chart. All tools were used and tested with other population of interests. In summary, STOPPFall scored the highest, satisfying all the criteria identified by the study. The scoring process is summarized in Table 3.2 as illustrated below.

Table 3.2 Fall Risk Assessment Tools Criteria Scoring Assessment

Fall Risk Assessment Tools	Assessment Criteria					Final Score
	Validity	Reproducibility	Equivalence	Feasibility	Acceptability	
DBI	1	1	1		1	4
DBI Calculator	1	1	1		1	4
Downtown	1	1			1	3
FRAT	1	1			1	3
STOPPFall	**1**	**1**	**1**	**1**	**1**	**5**
Hendrich II	1	1	1		1	4
JHFRAT	1	1		1	1	4
STEADI	1	1	1		1	4

3.2.1 STOPPFall Tool

Healthcare providers are frequently hesitant to deprescribe medications that increase the risk of falling (Laflamme et al., 2015; Seppala et al., 2019; Seppala et al., 2020).

Insufficient knowledge and competence are relevant barriers and even with systematic reviews, there is no common agreement on which drugs are classified FRIDs. Screening Tool of Older Persons Prescriptions in Older Adults with High Fall Risk (STOPPFall) and a deprescribing tool were created by European specialist panel to assist clinicians in the supervision of FRIDs and to enable the deprescribing mechanism (Seppala et al., 2020). The tool was designed by two mediators supported by evidence from current meta-analyses and Europe's national fall prevention standards (de Vries et al., 2018; Seppala et al., 2020). In three Delphi panel rotation, 24 experts selected their degree of agreement with the STOPPFall items on a Likert scale. From this, a 70% consensus threshold was picked. The expert participants were requested if some drugs are more likely to cause falls than others in the same pharmacological drug class. They were also inquired in a supplementary questionnaire in which instances of deprescribing of FRIDS must be taken into account and how it should be carried out. The panelists reached an agreement on 14 drug classes to be incorporated in the STOPPFall. Most of these were psychotropic drugs. The panelists indicated 18 differences among pharmacological subgroups in terms of fall risk-increasing properties. A feasible deprescribing scheme was constructed for STOPPFall drug classes aiming to enhance drug review (Seppala et al., 2020).

3.3 Pre and Post-intervention Demographic Profile

Pre-intervention (N=55) and post-intervention (N=58) pharmacy patient profiles were examined in the study. The average age of pre-intervention patients was 81 years, with a range of 74 to 88 years, whilst the average age post-intervention was 79 years, with a range between 75 and 86 years, indicating that the subjects of the study were older adults.

Females made up the majority of 65% (n=36) of the total, with males accounting for 35% (n=19) for pre-intervention and post-intervention, respectively, with females comprising 71% (n=41) and males of 29% (n=17). Hypertension, diabetes, and cardiovascular diseases such as congestive heart failure, atrial fibrillation, and ischemic heart disease were the most common comorbidities (Figure 3.1). The vast majority, primarily the females, fell and fractured for both pre (n=36) and post (n=41) intervention.

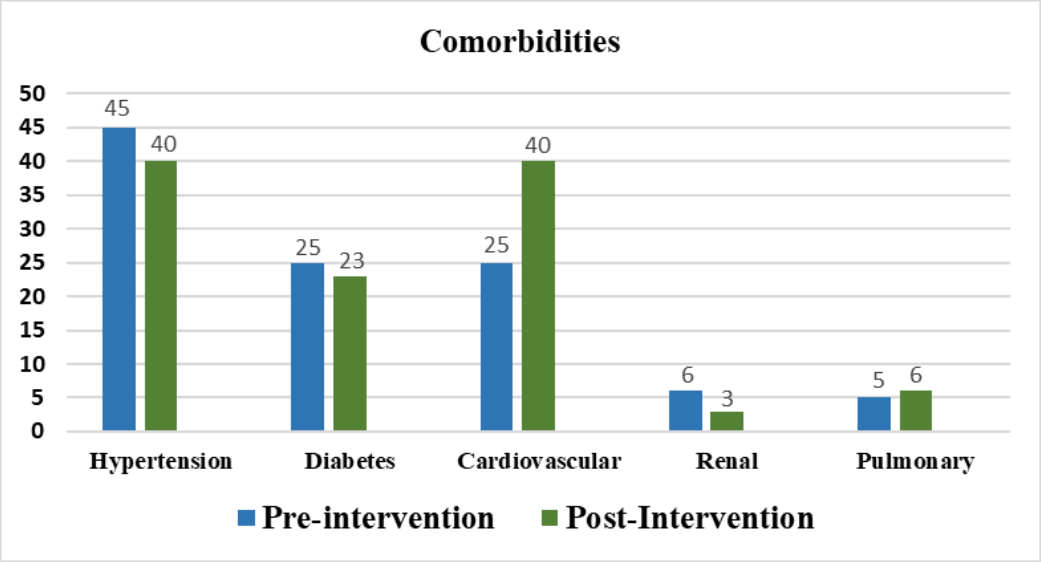

Figure 3.1 Pre-intervention (N=106) and Post-intervention (N=112) Comorbidities Profile

3.4 Pre and Post-intervention Prescribed Fall Risk-increasing Drugs

Figure 3.2 depicts the most usually prescribed fall risk-increasing drugs during pre (N=162) and post (N=181) intervention assessments. The most commonly prescribed drugs for pre-intervention were antidepressants (n=35), diuretics (n=34), opioids (n=31), and

benzodiazepines (n=23), whilst diuretics (n=41), opioids (n=39), and antidepressants (n=26) were frequently prescribed for post-intervention.

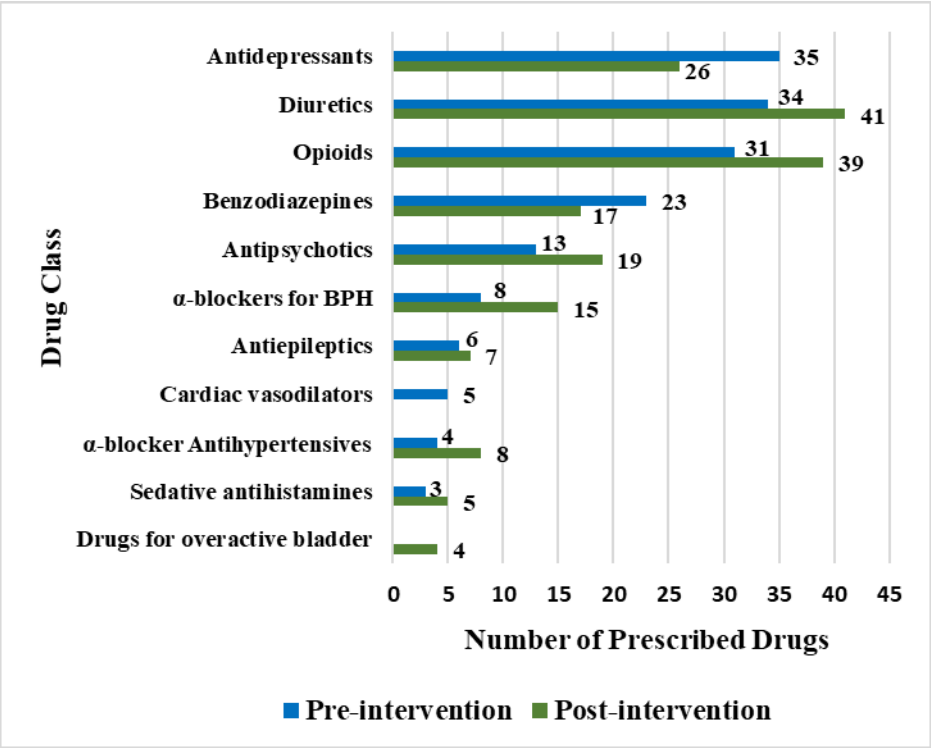

Figure 3.2 Number of Prescribed Fall Risk-increasing Drugs of Pre-intervention (N=162) and Post-intervention (N=181)

3.5 Pre and Post-intervention Deprescribing Profile

The most deprescribed drugs, as shown in figure 3.3, were sedative antihistamines which were completely discontinued, followed by opioids and benzodiazepines. Whereas α-blocker antihypertensives were the drugs with the highest non-deprescription rate, antiepileptics and antidepressants had the same percentage for both documented and not documented, respectively. Figure 3.4 of post-intervention shows that opioids had the highest percentage of deprescribing, preceded by sedative antihistamines and antipsychotics. Antiepileptics received the highest percentage in the non-deprescribing category, accompanied by α-blockers for BPH and α-blockers antihypertensives.

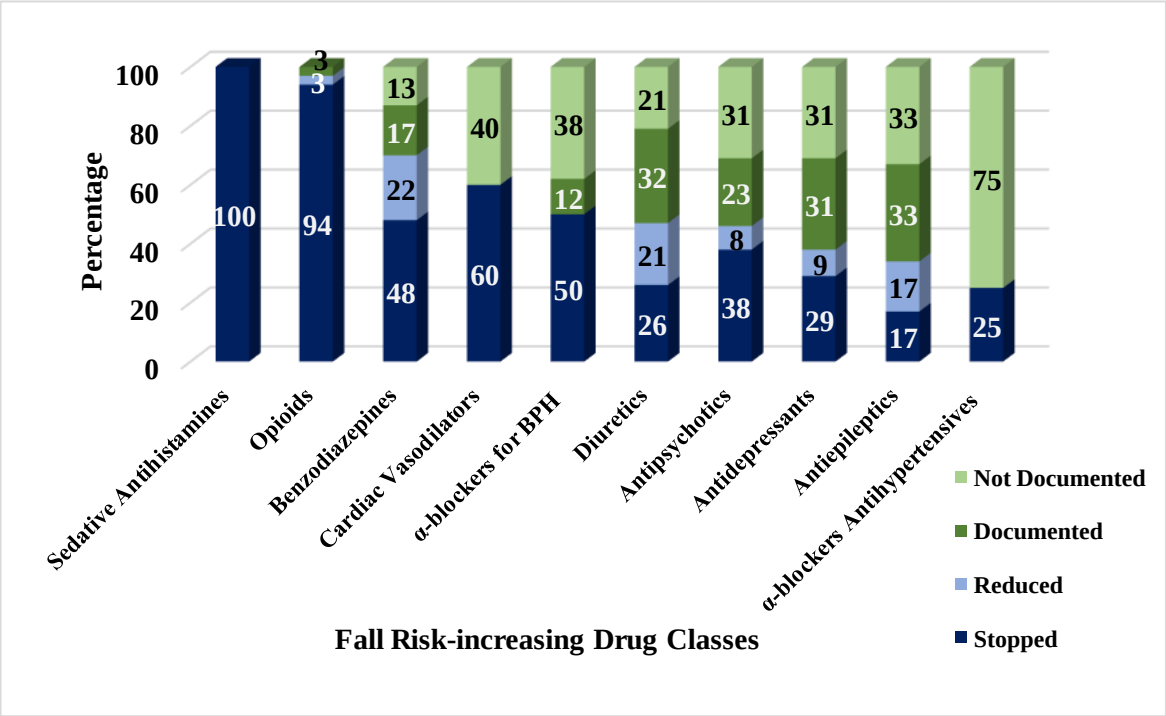

Figure 3.3 Pre-intervention Deprescribing Profile

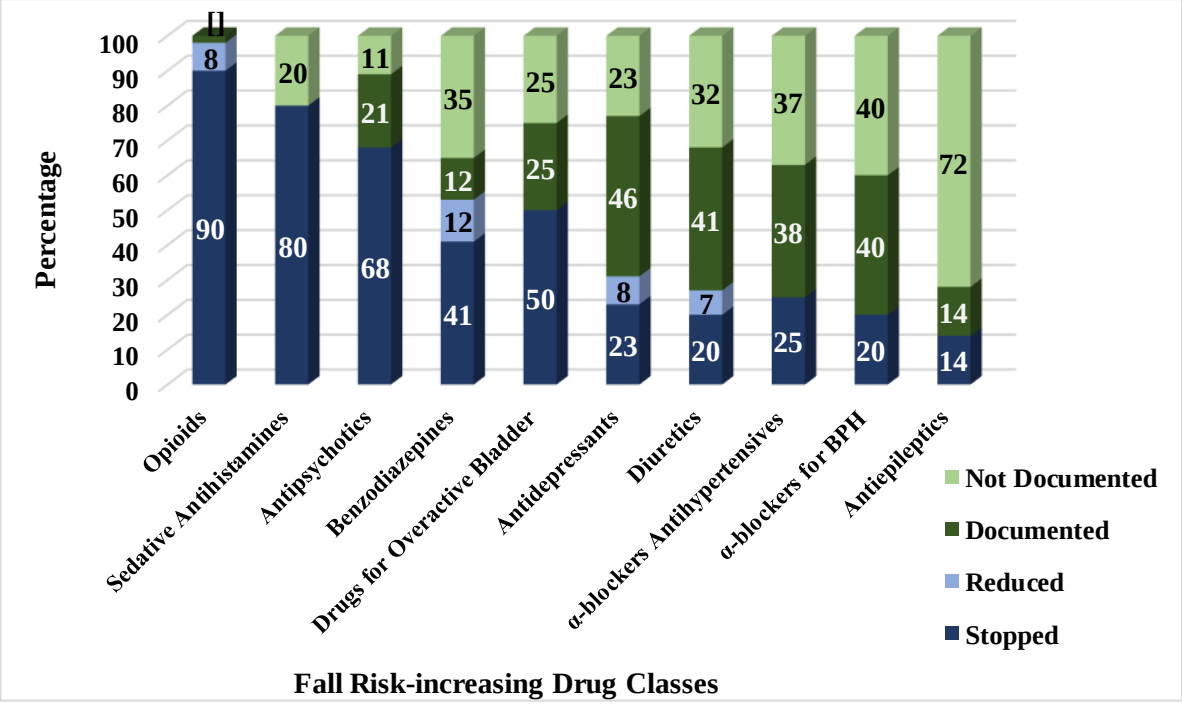

Figure 3.4 Post-intervention Deprescribing Profile

3.6 Pre-Intervention Deprescription Rate

In terms of deprescription rate as shown in Table 3.3a by t-test for one proportion, opioids (97%, p<0.01) and benzodiazepines (70%, P=0.030) have significantly higher deprescription rate, whereas diuretics (47%), antipsychotics (46%) and antidepressants (37%) signify lower deprescription rate as their p value is >0.05. Other drugs in table 3.3b such as sedative antihistamines, cardiac vasodilators, and α-blockers for Benign Prostate Hyperplasia (BPH) indicate a high deprescription rate, whilst anti-epileptic and α-blockers antihypertensives demonstrate a low deprescription rate. In all these drug classes, the sample size was too small to generate a reliable conclusion.

Table 3.3a Pre-intervention Deprescription Rate

FRIDS	Opioids	BZDs	Diuretics	Antipsychotics	Antidepressants
Total No. of Drugs	n=31	n=23	n=34	n=13	n=35
Deprescribed Drugs	30	16	16	6	13
Deprescribed Rate (%)	97	70	47	46	37
p-value	<0.01	0.030	0.630	0.610	0.940

FRIDS- Fall Risk-increasing Drugs
BZDs-Benzodiazepines

Table 3.3b Pre-intervention Deprescription Rate

FRIDs	Sedative Antihistamines	Cardiac Vasodilators	α-blockers for BPH	Antiepileptics	α-blockers Antihypertensives
Total No. of Drugs	n=3	n=5	n=8	n=6	n=4
Deprescribed Drugs	3	3	4	2	1
Deprescribed Rate (%)	100	60	50	33	25

BPH- Benign Prostate Hyperplasia
FRIDS- Fall Risk-increasing Drugs

3.7 Post-intervention Deprescription Rate

In terms of deprescription rate for post-intervention as depicted in Table 3.4a, by using t-test for one proportion, it shows that only the opioids (97%, $p<0.01$) and antipsychotics (68.42%, $p=0.027$) were statistically higher than 50% suggesting that these medications were deprescribed more as compared to other medications. Among the drugs in Table 3.4b, by using percentage, sedative antihistamines (80%) have the highest deprescription rate, followed by α-blockers antihypertensives (25%), α-blockers for BPH (20%) and antiepileptics (14%).

Table 3.4a Post-intervention Deprescription Rate

FRIDs	Opioids	Antipsychotics	BZDs	Antidepressants	Diuretics
Total No. of Drugs	n=39	n=19	n=17	n=26	n=41
Deprescribed Drugs	38	13	9	8	11
Deprescribed Rate (%)	97	68	53	31	27
p-value	<0.01	0.027	0.404	0.975	0.998

BZDs-Benzodiazepines
FRIDs- Fall Risk-increasing Drugs

Table 3.4b Post-intervention Deprescription Rate

FRIDs	Sedative Antihistamines	α-blockers Antihypertensives	α-blockers for BPH	Antiepileptics
Total No. of Drugs	n=5	n=8	n=15	n=7
Deprescribed Drugs	4	2	3	1
Deprescribed Rate (%)	80	25	20	14

BPH-Benign Prostate Hyperplasia
FRIDs-Fall Risk-increasing Drugs

3.8 Researcher's Intervention

The researcher presented the chosen fall risk-assessment tool (STOPPFall) to the clinical pharmacists at Karin Grech Hospital during Falls Prevention Week in September 2021, with nine participants, six females and three males.

3.9 Deprescription Rate of Pre-intervention versus Post-intervention Studies

The intervention revealed that the deprescription rates did not improve significantly when comparing the deprescription rate of the pre- and post-assessment, as presented in Table 3.5 This means that there was no change in the deprescription rate after the tool was implemented as it will take more time and exposure to the intervention for the intended change to be statistically determined.

Table 3.5 Deprescription Rate of Pre-intervention versus Post-intervention Study

Deprescribed Drug Classes	Pre-intervention N=162		Post-intervention N=181		p-value
	Total No. of Drugs	Deprescribed Drugs (Reduced + Stopped)	Total No. of Drugs	Deprescribed Drugs (Reduced + Stopped)	
Antidepressants	35	13	26	8	0.302
Diuretics	34	16	41	11	0.035
Opioids	31	30	39	38	0.434
Benzodiazepines	23	16	17	9	0.142
Antipsychotics	13	6	19	13	0.104
α-blockers for BPH	8	4	15	3	0.068
Antiepileptics	6	2	7	1	0.208
Cardiac Vasodilators	5	3	0	0	-
α- blockers Antihypertensives	4	1	8	2	0.500
Sedative Antihistamines	3	3	5	4	0.204
Drugs for Overactive bladder	0	0	4	2	-

3.10 Clinical Pharmacists Risk Drug-induced Falls Documentation

The clinical pharmacists are required to document a care issue for drugs that should be considered for deprescribing. Table 3.6 shows the extent of documentation for non-deprescribed drugs. There was no significant improvement in the rate of documentation when comparing the pre- and post-intervention study.

Table 3.6 Rate of Risk Drug-induced Falls Documentation

Deprescribed Drug Classes	Pre-intervention N=68			Post-intervention N=90			p-value
	Total of NDD	Documented	%	Total of NDD	Documented	%	
Antidepressants	22	11	50	18	12	66.67	0.144
Diuretics	18	11	61.11	30	17	56.67	0.381
Antipsychotics	7	3	42.86	6	4	66.67	0.195
Benzodiazepines	7	4	57.14	8	2	25	0.102
α-blockers for BPH	4	1	25	12	6	50	-
Antiepileptics	4	2	50	6	1	16.67	0.130
α-blockers Antihypertensives	3	0	0	6	3	50	0.067
Cardiac Vasodilators	2	0	0	0	0	-	-
Opioids	1	1	100	1	1	100	-
Drugs for Overactive bladder	0	0	-	2	1	50	-
Sedative Antihistamines	0	0	-	1	0	0	-

BPH- alpha blockers for Benign Prostate Hyperplasia
NDD- Non-deprescribed drugs
%- Rate of Documentation

Chapter 4

Discussion

4.1 Patient-centric Environment

Rehabilitation is a vital intervention for the older adults due to the increased prevalence of impairment. A rehabilitation team's composition varies according to local services, the mix of accessible expertise and the requirements of the client group. A core involvement of physicians, nurses, physiotherapists, and occupational therapists is typical. The contribution of caregivers and patients in the rehabilitation program should not be overlooked because results are typically better when they are involved and engaged (Stott & Quinn, 2016). Clinical pharmacists take an active role in patient care by interacting with other members of the healthcare team to promote safe and effective drug use (Stuchbery et al., 2007; Mamo et al., 2014). Pharmacists advise physicians in a wide range of hospital environments on medication dosing and administration, current evidence-based treatment care standards, ADRs, intravenous drug compatibility, drug interactions and other medication-related issues (Viktil, 2008; Mamo et al., 2014).

KGH pharmacy services adhere to a practise ideology that centres on being safe, individual patient-focused, collaborative and inter-disciplinary, evidence-based, and cost-effective in all endeavours and programs. The pharmacists are delegated to the wards and actively engage in quality care by maintaining up-to-date pharmacy patient profiles that are used throughout weekly consultant-led ward rounds to optimise the patient's drug treatment and reduce medication administration errors, keeping themselves accessible and communicating with patients and carers to confirm medication history, and counselling patients at discharge.[9]

[9] Government of Malta. Pharmy [Internet] Malta: health.gov.mt; [cited 2022 Apr 12]. Available: https://deputyprimeminister.gov.mt/en/kgrh/Pages/pharmacy.aspx

The patient-centric environment where the study was conducted becomes a channel, denoting that a multidisciplinary approach not only forms alliances with healthcare practitioners but foremost with patients and their families, in order to arrive at decision-making with the expertise's guidance to suit the wants, needs, and preferences of the patients without compromising their health status. The approach entails providing patients with education and support as a journey, which may produce a holistic rehabilitative effect for it does not only target the physical and physiological state but empowers the patient's mind and being by constructing significant decisions to participate in their own care. Involving patients in these shared decision-making positions make them in an active state, which may enhance compliance with the treatment plan regardless of their current condition. Participating helps these older people feel better about themselves and more confident that their opinions continue to be valued.

4.2 Deprescribing Tool: A Pharmacovigilance Mechanism

Objective assessments of inappropriate prescribing (e.g., STOPP/STOPPFrail criteria and the Beers' criteria) are vital patient care safety tools and a valuable potential means of recognising who may benefit from deprescribing (Spencer & Campbell, 2014; Duncan et al., 2017). Many clinical tools are readily accessible to help clinicians with deprescribing. They differ greatly in type, are both general or multifactorial and drug-specific, with the latter focusing on a narrow range of drug classes. The mechanism of innovation of the tools differs considerably and few were investigated in clinical practice. As a result, it is unclear which of these tools will have the greatest impact in terms of increasing deprescribing and improving clinical outcomes (Reeve, 2020). Tools possess "explicit" and "implicit" criteria, where explicit tools list the medications to be evaluated for drug review, whereas implicit

tools propose questions a clinician may want to start to determine whether a drug is still necessary or appropriate (Spinewine, 2007; Le, 2019).

The chosen tool (STOPPFall) is a deprescribing tool that provides workable instruction to make the discontinuation of FRIDs convenient and more systematic. The tool also consists of a questionnaire that directs pharmacists on when to withdraw medications based on scientific evidence and rigorously validated by geriatric and pharmacology experts (Seppala et al., 2020). The STOPPFall tool embodies both the explicit and implicit mechanisms to facilitate detection of drugs that increase the risk of falling. The mechanisms built into this tool have their own pharmacovigilance nature which is heightened by the clinicians' pharmacovigilance task. The tool was a new guide that was incorporated into clinical pharmacists' deprescribing activities. The deprescribing tool should motivate clinical pharmacists and the entire healthcare team in creating decisions by conquering doubts and hesitancy in the clinical setting, as it provides objective evidence with a stepwise approach. In this way, the risks can be minimised and managed with right planning, monitoring and re-initiation of treatment when need arises.

4.3 Deprescribing: An Integrated Pharmacovigilance Role

According to a 2018 UK teaching hospital deprescribing review, only 4% of patients had their treatment deprescribed prior to admission, implying a demand to modify healthcare practitioners' behaviour to accommodate regular deprescribing in hospitals (Scott et al., 2019). Individuals in nursing homes are more likely to be at a stage where deprescribing is suggested. Deprescribing is important in other clinical settings, particularly given that more than one-third of older patients received inappropriate prescribing (Moriarty et al., 2015;

Duncan et al., 2017). General practitioners (GPs) are better placed to facilitate deprescribing provided there is access to the patient's complete medical record, which includes diagnoses, investigations, and current and drug history, to better inform treatment decisions and form a connection with the patient that instils trust and reinforces shared decision-making (Reeve et al., 2013; Duncan et al., 2017). However, deprescribing by GPs is often limited due to a lack of shared patient information between hospitals and community practice. This is particularly the case in Malta where to date, sharing of complete medical records is lacking.

A myriad of other healthcare providers who may have a lot of time to devote to a prescribing evaluation can also assist GPs make deprescribing judgements. Nurse practitioners frequently play a pivotal role in supervising common long-term situations in which nurse-led deprescribing initiatives have a significant influence on primary care (Brandt, 2016; Duncan et al., 2017). Clinical pharmacist drug therapy reviews have been shown to lower the number of medications prescribed (Holland et al., 2008; Duncan et al., 2017). A cluster randomised trial called the PINCER trial demonstrated that a pharmacist-led intervention in the general health environment could reduce unsafe prescribing (Avery et al., 2012; Duncan et al., 2017). An example of a specific type of intervention are medication use reviews (MURs), an organised adherence focused assessment for patients in long-term conditions subject to polypharmacy (Holland et al., 2008; Duncan et al., 2017). Whilst consultants are typically responsible for ongoing treatment reviews for chronic diseases, hospital clinicians such as clinical pharmacists and generalist doctors can impart to deprescribing, and other hospital-based intervention programs to discontinue unnecessary drugs for admitted older patients.

The utilisation of a patient-centred, interdisciplinary framework entailing physicians, nurses, pharmacists, and residents is essential to effective deprescribing (Reeve et al., 2015; Ailabouni et al., 2017). Nurses play a crucial role in the care of older people in residential care institutions. As shown in a cross-sectional survey of registered nurses'(RNs) views on deprescribing and the role of clinical pharmacists, RNs not only recognise pharmacists' competence, but they also firmly believe that pharmacists contribute an essential function in all aspects of the deprescribing process. More than half (67.4%) of these nurses agreed or strongly agreed that deprescribing with the guidance of a clinical pharmacist was advantageous to residents and could strengthen drug therapy compliance (44%), residents' life quality (50.5%), and the duration of time nurse practitioners invested on drug administration (35.2%). Nurses and pharmacists can collaborate to showcase patient-specific deprescribing proposals to GPs, along with clear reasons and purpose such as suspected ADRs observed by RNs while checking residents (Ailabouni et al., 2017).

4.4 Acclimatizing Health Systems

According to Shore et al. (2016), changes prompted by professionals were regarded as simple and easy to implement and met little resistance from health care practitioners. Institutional changes that have been clearly conveyed to allow for planning have increased the likelihood of success. In a study by Nilsen et al. (2020), healthcare practitioners stressed the relevance of having the potential to shape organisational restructuring that is implemented. Further, Leape et al. (2006) posited that introducing practices that have been demonstrated to help lower errors, is a pivotal step in attaining a safe culture within healthcare institutions. Even just a brief assessment of hospital care indicates the demand for a multitude of these "safe practices" (Leape et al., 2006).

According to Brewster et al. (2015), new practices provide employees with intrinsic fulfilment. When placed in scenarios where these new practices were gratifying to the team, the behaviours and norms evolved over time into effective integration methods. Many such advancements have been observed, such as follow-up phone conversations with discharged patients, individualised patient education, multidisciplinary rounds to facilitate treatment for specific patients and plan for discharge, and collaboration with post-acute providers to arrange the care transition process. With regard to adapting new system, it was difficult for the personnel to reap the benefits of an innovation instantaneously. This compelled the accumulation of first-hand proof over for at least several months, which gradually changed members' orientation and managed to persuade them to self-reinforce the new practice (Brewster et al., 2015).

In the systematic review study by Belkora et al. (2008), as cited in Geerligs et al. (2018), interventions that complement the current inpatient and outpatient hospital systems and working practises were considered viable, whereas interventions that come up with innovative solutions and standard processes were more prone to delays, operational lag, and gaps. These issues could be conquered through versatile and repetitive interventions, including those that involve in continuing review and tailoring (Belkora et al., 2008; Geerligs et al., 2018). Action research methodologies and frameworks' utilisation assisted this process by allowing research to answer issues and make real-time intervention changes (Moody et al., 2001; Geerligs et al., 2018). The complex nature of the intervention results in more challenging integration. Where interventions entailed the installation of new operating processes, IT features and ease of access were frequently reported. Interventions incorporating supplemental forms or screening tools contribute to staff workload and raise

the risk of process errors. This issue can be managed by streamlining forms and tools to create a more user-friendly task. Interventions that were viewed as simple and convenient to enforce were far more likely to acquire favourable acceptance and increased participation in the execution process (Schmied et al., 2011; Geerligs et al., 2018).

Clinical pharmacists in KGH performed deprescribing before the selected tool was introduced to them. Opioids and benzodiazepines were the most commonly deprescribed drug classes. After using the tool for the three months, it was observed that there was still a consistent pattern of deprescribing opioids, this time in conjunction with antipsychotic drugs. The overall impact of introducing a new tool (STOPPFall) into the system would take time and definitely several months to years to see the strength of its effect. Some clinical pharmacists made comments during the documentation of the pharmaceutical issues to watch the dose of specific drugs that increase the risk of falls. Making such initiative indicates acceptance of the new approach, which will be gradually integrated into the system. Clinical pharmacists' complete acceptance of the system signifies empowerment and support from the administration and the entire healthcare team. Empowerment motivates both leaders and subordinates to carry out their pharmacovigilance tasks to do the best of their potential and to take pride in working. An empowered healthcare provider is destined for achievement because of continuous growth and sense of purpose.

Empowered clinical pharmacists would be capable of exercising their pharmacovigilance role in safeguarding patients' welfare as a result of using the selected clinical tool, enabling them to contribute to the enhancement of their quality of life upon discharge and be fully rehabilitated at home. Whilst the patient and hospital benefits with the deprescribing

service, family members can experience ease and satisfaction with the therapeutic plan given. Thus, an empowered clinical pharmacist also empowers the patient in totality.

4.5 Challenges to Deprescribing

Studies show that deprescribing challenges are categorized into three main areas: patient-related issues, healthcare related-system, and healthcare providers relationship**.**

In the study of Wu et al. (2021), patients were found to have had limited health literacy and were hesitant to discontinue medications due to fictitious views. Patients are frequently treated without a say in the drug-use decision-making process. Another patient-related issue was withholding of significant information on ADRs which patients associate in their aging status. Other possible causes include cognitive deterioration, operational dependency, and educational background which affects the patient's ability to explain the concerns about the ongoing treatment and the need for deprescribing (Schuling et al., 2012; Ni Chróinín et al., 2015; Cullinan et al., 2016).

Other barriers to successful deprescribing involve the patient's mindset or overconfidence on the efficacy and ease of using medications instead of lifestyle modification (Dharmarajan et al., 2019).

Wu et. al. (2021) cited the research conducted by Cognitive Decline Partnership Centre, Sydney (2019) highlighting that the challenges to deprescribing related to healthcare providers involves the increasing number of older patients with complex multiple comorbidities, insufficient number and guidance from in-house healthcare providers in prescribing, and medication counselling involving polypharmacy. Multiple healthcare

practitioners are needed in the care of older patients, which leads to sovereignty in the patient's therapeutic intervention according to their scope and expertise.

The interprofessional dynamics within a healthcare setting also has some issues affecting deprescribing such as the lack of effective collaboration illustrated in the physician's dominance in managing the medical treatment. Some doctors firmly believe in having a governing role in assessing the patient's clinical therapy that includes reducing doses, quantifying drug usage, and cutting the list of inappropriate drugs but an added burden on top of their daily duties (Palagyi et al., 2016; Cullinan et al., 2016).

Another challenge is the hesitancy to change a prescription recommended by a colleague or a specialist. In other instances, junior doctors stress that consultants and GPs are the leading medical professionals held to account for deprescribing followed by senior house officers, junior doctors, and pharmacists (Jubraj et al., 2015; Cullinan et al., 2016). Poor documentation is another constraint to deprescribing because it blocks the understanding of other physician's intentions for engaging a particular treatment plan. The possibility to obtain a current list of patients' treatment complicates it as there is a demand to contact multiple sources such as patients, family, pharmacy, and GP, and unpredictability as to which origin offers the best list of medications administered to the patient (Shemeili et al., 2015; Cullinan et al., 2016).

As pointed out during the Bruyère Evidence-Based Deprescribing Guideline symposium (2018) held in Ontario, Canada, allied medical practitioners are sometimes excluded from circles or decision-making which poses a challenge to endorse deprescribing. Healthcare providers also have problems communicating across disciplines, specializations, and

clinical settings which can impede the actualization of deprescribing practices. Other concerns about deprescribing are explicitly associated with particular health-care settings. HCPs situated in long-term care facilities have massive workloads and scarce resources, which includes time. Most settings and institutions do not have regulations in place to encourage therapeutic reviews or deprescribing. Deprescribing is not yet a top concern for some organisations, hence a partial drive to develop and enact deprescribing measures. Financial systems and profit-related incentives can limit enforcement of deprescribing guidelines. An inadequate myriad of guidelines is currently available and the recommendations that do prevail may not always contain non-pharmacological schemes for patient management, and some perceive that scientific evidence relating to the standards is limited. Prescribing guidelines are well-supported and widely disseminated but seldom involve details on deprescribing (Conklin et al., 2018).

4.6 Overcoming Challenges

One of the proposed methods for rational medication use for patients in the Global Safety Challenge on Medication Safety in Geneva by the World Health Organization in 2017, is the provision of teaching materials and tools (e.g., drug passports or personalised medication records) to raise patient understanding about inappropriate medications and help them realise the pros and cons of each treatment would be beneficial to them (Wu et al., 2021). Bruyère Evidence-Based Deprescribing Guideline Symposium (2018) suggested to involve and motivate patients to take an active part in their medical care in order to properly handle treatments on their own; specified patients, caregivers, and members of the public must participate in the innovation, evaluation and application of guidelines and form

deprescribing advocacy organisations which have the strength to utilize authentic influence (Conklin et al., 2018).

Setting goals through clear procedures and accountabilities will improve communication among interprofessional. It should be clearly defined who has the absolute obligation for securing the correctness of a patient's medical care, strengthening drug review procedures, and effectively educating new breed doctors (Cullinan et al., 2016). Other suggestions include providing tools, recommendations or guidelines, and academic resources on how to manage polypharmacy in older people; developing institutional curricula for medical courses on drug safety management and deprescribing, incentivizing health practitioners who perform a therapeutic plan review as part of a regular health screening (Kashyap et al., 2019; Ng et al., 2021).

In 2018, Bruyère Evidence-Based Deprescribing Guideline Symposium emphasized that collaboration of researchers and HCPs from different fields to work together, have annual conferences, set up and support an online network system, and reinforce opinion leaders who can come up with new ideas on solving deprescribing problems in healthcare system are highly encouraged (Conklin et al., 2018). Wu et al. (2021) also suggested that a national deprescribing group should be formed to develop techniques, standards, and initiative plans for polypharmacy and deprescribing in older adults.

4.7 Proposed Model for Deprescribing of Fall Risk-increasing Drugs

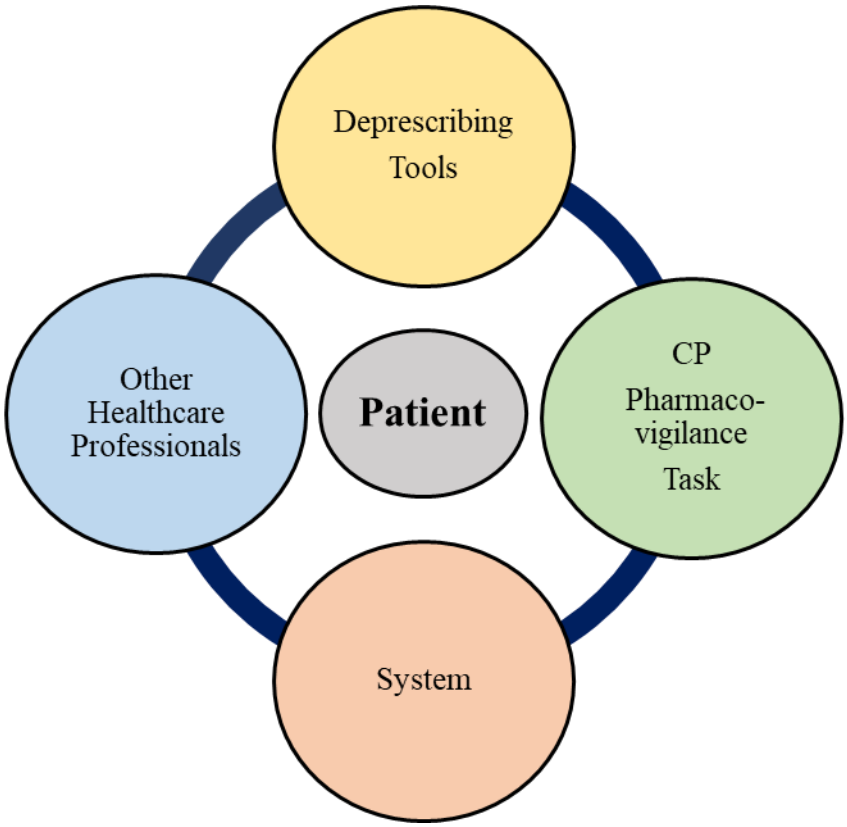

Figure 4.1 Proposed Model for Deprescribing of Fall Risk-increasing Drugs

The proposed model (Figure 4.7) illustrates the four key components in enforcing a pharmacovigilance process in a patient-centric environment. The patient in the centre is the focal point that connects all the components. Deprescribing tool as a first component is a pharmacovigilance method that provides an opportunity for healthcare providers to improve the outcome and quality of life for older patients. Initiating deprescribing could be best possibly realised using a screening or clinical tool (STOPPFall) for an easy, systematic, and evidence-based guide to prevent drug-related falls. A tool that is quickly generated, dependable, and contains substantial proof information could assist the clinician in becoming a more active participant in the deprescribing process, with the goal of

lowering total costs whilst working to improve outcomes. The second component is the pharmacovigilance task of pharmacists, which emphasises the clinical pharmacist's (CPs) role in ensuring a safe and efficacious dose by implementing deprescribing. This function gives them the authority to connect with the patient, carers, and other healthcare providers (e.g., consultants, nurses, physical therapists etc.) to develop an effective therapeutic plan. The third component to consider is other healthcare professionals (consultants or GPs, nurses etc.) for a collaborative agreement on deprescribing. Starting a successful deprescribing program requires a multidisciplinary approach with the goal of reducing or, if possible, eliminating drug-related falls and optimising medication. Effective communication among these healthcare members fosters a supportive environment in which to establish the best therapeutic plan for older patients without concern of professional hierarchy or bureaucracy. The fourth essential component for deprescribing to thrive is the system. A patient-centric culture must be embedded in the system, in order for deprescribing to be actualised through shared decision making. Clinicians and patients cooperate to establish therapeutic choices and evidence-based clinical plans based on patients' preferences and beliefs without jeopardising their health status. Increasing administration support for the deprescribing process by providing resources, training, and incentives encourages healthcare members to take on more responsibilities because hard work is rewarded and valued.

4.8 Limitations of the Study

The study only gathered a small number of pharmacy patient profiles for both the pre-intervention and post-intervention phases because several profiles were excluded from the criteria, mainly because a fall was reported to be mechanical. This was a retrospective

study, no confirmation with the patient was possible. The coverage for each collection was limited to a few months, particularly the post-intervention which lasted only for three months from October 2021 to January 2022. Clinical notes and pharmacy patient profiles are paper-based, whereas the selected tool is an electronic data-based source. This difference in the medium may introduce a barrier to the seamless use during clinical practice of the STOPPFall tool.

4.9 Recommendations

A wide range of coverage of the collection of patient profiles for more than six months to one year is suggested as the results will give a more definite trend and movement on deprescribing activity. Another proposal is to incorporate a fall risk assessment tool that must be completed on admission for each patient as part of the standard clinical practice and documented in the patient's clinical notes. It is also suggested that the study is carried out in different healthcare settings namely nursing homes, long-term facilities, and ambulatory centres because some of these facilities, particularly nursing care centres, do not have regular access to clinical pharmacy services. Future research studies may assess the impact of different interventions including a second intervention and infographics about application of FRATs in clinical pharmacy practice.

4.10 Conclusion

The research led to an application of the selected medication-based fall risk assessment tool within the KGH pharmacy department to evaluate the degree of deprescribing conducted for older patients at risk of falling. A model was proposed as part of the clinical pharmacist medication risk management for falls in older patients.

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Appendices

Appendix 1

Ethics Approval

Dear Ms Fernandez,

Good morning and apologies for the late reply, but we are really caught up at the moment with the September examinations coming.

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.

Kindly **confirm** that you sent all the documents which you attached to the UREC form together with other documents related to your study.

Kindly note that these documents are also requested for audit purposes.

Regards,
Annalise

L-Università ta' Malta

Annalise Mallia Duca | Secretary

Faculty Research Ethics Committee
Faculty of Medicine and Surgery
Medical School, Mater Dei Hospital
+356 2340 1803

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

Appendix 2

Criteria for Selection of Fall Risk Assessment Tool

Description	Tool	Models		Methods of measure		Statistical Tools Used								
DIFFERENT FALL RISK ASSESSMENT	Availability	Multifactorial	Medication-related	Reliability	Validity	Delphi Method	Sensitivity	Specificity	Positive Predictive Validity	Negative Predictive Validity	AUC	Interrater reliability	Statistics (Frequency, Mean, Ranges & Standard	Hazard Ratio
JHFRAT	✓	✓		✓	✓		78%	83%	30.8%	91.4%	0.708	0.96		
Downton	✓	✓		✓	✓		92%	36%	33%	93%		1.40		
Heindrich II FRM	✓	✓		✓	✓		78.72%	64.07%			0.765			
FRAT	✓	✓		✓	✓		>70%	>70%						
STEADI	✓	✓		✓	✓		65%	65%						
STOPPFall	✓		✓	✓	✓	✓								
IMPROveFALL			✓	✓	✓									Intervention to first fall (HR 1.17;95%CI 0.89-1.54 Time to second fall (1.19;0.78-1.82) Time to first fall-related GP-consultation (0.66; 0.42-1.06) Time to first fall-related ED-visit (0.85;0.43-1.68)

Appendix 2

Criteria for Selection of Fall Risk Assessment Tool (Cont.)

Description	Tool	Models		Methods of measure		Statistical Tools Used								
DIFFERENT FALL RISK ASSESSMENT	Availability	Multifactorial	Medication-related	Reliability	Validity	Delphi Method	Sensitivity	Specificity	Positive Predictive Validity	Negative Predictive Validity	AUC	Interrater reliability	Descriptive Statistics (Frequency, Mean, Ranges & Standard Deviation)	Hazard Ratio
DBI	✓		✓	✓	✓							1.90		
DBI Calculator	✓		✓		✓		100%							
Two-Stage Model (FASPIP)→			✓			✓								
Inclusion of medication-related in fall risk assessment tool			✓										Active substances=47% high risk of category A for increasing fall risk Fall experienced patients (n=188)	

The Downton Fall Risk Index (Downton)

Title	Components	Medicines	Scoring	Tested for:	Applied in	Strength	Weakness
Downton	-previous falls -medications -sensory disability [visual or hearing impairment, impaired motor skills (reduced muscle strength or loss of function in a limb)] -cognitive disability (orientation to time, place, and person) - walking ability (unsafe gait)	-tranquilizers -sedatives -diuretics -antihypertensives -antiparkinsonian drugs -antidepressants	Scores for each risk factor are added to produce an index sum (range 0 – 11; DFRI score). -A score of three or greater is taken to indicate a high risk of fall	Description of the characteristics of the included studies were tabulated and presented in terms of: -Absolute and relative frequencies -sensitivities -specificities -negative predictive values -positive predictive values and corresponding 95% confidence intervals	Geriatric rehabilitation hospital	-predicted severe clinical outcomes such as fall-related injury, head injury, hip fracture and death -Validation of the Downton index among patients in geriatric rehabilitation showed a **sensitivity of 92%** -five of eleven risk items of DFRI reflect medication as a predisposing factor and when added together to form a sub-score of the index, they were significantly associated with the fall risk factor -easy to administer and includes many items that can be obtained from medical records	-DFRI did not show better prediction accuracy when falls judged as precipitated by acute illness, acute disease and side effects from a recently prescribed drug were excluded - demonstrated only 50% of predictive accuracy -demonstrated only 36% of specificity -no interrater reliability study conducted

Fall Risk Assessment Tool (FRAT)

Title	Components	Medicines	Scoring	Tested for:	Applied in	Strength	Weakness
FRAT	-Recent falls -medications -psychological -cognitive status -vision -mobility - transfers behaviour ADL, environment, nutrition, continence, other (osteoporosis, history of fracture/s)	-Sedatives -Anti-depressants -Anti-Parkinson's -Diuretics Antihypertensives -Hypnotics	-Not taking any of these=1 - Taking one=2 - Taking two=3 - Taking more than 2=4	->70% of sensitivity and specificity	Subacute Care and Rehabilitation Setting	-high predictive accuracy -no training required to administer the tool -this tool has been reviewed through a systematic search for the evidence, assessment of relevance to specific settings and assessment of quality using validated tools -The Falls Risk Assessment Tool (FRAT) was developed by the Peninsula Health Falls Prevention Service for a DH funded project in 1999, and is part of the FRAT Pack. A study evaluating the reliability and validity of the FRAT has been published (Stapleton C, Hough P, Bull K, Hill K, Greenwood K, Oldmeadow L (2009).	-the tool is not specific to medication-related for it is a multifactorial risk assessment tool -scarcity of evidence regarding the use of falls risk assessment tools across different settings

John Hopkins Fall Risk Assessment Tool (JHFRAT)

Title	Components	Medicines	Scoring	Tested for	Applied in	Strength	Weakness
JHFRAT	-Age -Fall History -Elimination (bowel and urine) -Medications -Patient care -Equipment -Mobility -Cognition	-PCA/Opiates - anticonvulsants, -anti-hypertensives -diuretics -hypnotics -laxatives -sedatives psychotropics	1 high fall risk drug=3points 2 or more high fall risk drugs=5 points Sedated procedure within past 24 hrs= 7 points	-reliability (reproducibility of results) -construct validity (measures fall risk) -predictive validity (extent to which risk score predicts a fall) -AUC is above .7 which is .708	-Academic medical center	-high levels of tool acceptability achieved in more than 100 hospitals AUC is .708 (in the study conducted by Keum Soon Kim et al. 2011) which conclude that the tool has decisive power -adapted and validated by different countries (Spain, Korea and US etc.)	- psychometric qualities are not yet well-established for application in acute care. - Due to changes and discontinuation of medication orders, the interrater agreement was low, implying that dual-rater agreement on medication was less than satisfactory. Variations in medication scale items could also be attributed to how as needed drugs are scored, with some staff nurses only scoring this item when the patient is actively taking the medication. -It is not a medication-specific tool

The Drug Burden Index Calculator

Title	Components	Medicines	Scoring	Tested for:	Applied in	Strength	Weakness
DBI CALCULATOR	$DBI = \sum \frac{D}{\delta + D}$ **D** = daily dose of an individual drug δ = minimum recommended daily dose of the individual drug. $\sum$ = *indicates that the DBI is the sum score of prescribed drugs with probable anticholinergic and sedative properties for each patient* *Ex.* *A patient who takes 10mg Temazepam each night* *-minimum licensed dose on the US Food and Drug Administration label of 7.5mg* *Hence (10/10+7.5)=0.57* *DBI=0.57*	- anticholinergic -sedatives	-In performing the DBI calculation, each drug (ingredient) has a DBI SCORE *between 0 and 1*	Evaluation Phase (evaluated by 10 accredited pharmacist participants): - Performance task - Usability survey Cohen's Kappa Sensitivity Test	-evaluated by 10 accredited pharmacist participants in a controlled setting	-Electronic DBI calculators have been developed to inform clinicians of their patient's DBI and its associated risks Sensitivity compared with manual calculation was 100% when DBI for the individual drug or total DBI score for the case was equal to zero -DBI calculators and reports could be integrated into electronic prescribing through CDSS -can be calculated for any older person where accurate information on their medication use including dose is available using the local formulary-	-limited to medications with anticholinergic and sedative effects -reduced accuracy was observed for drug products that contain two or more active ingredients contributing to DBI and drug products which have longer than 24-hour dosing formulations (eg. Extended-release patches -only 50% of participants agreed that the application provided enough information to make a clinical decision which they consult other sources.

Drug Burden Index (DBI)

Title	Components	Medicines	Scoring	Tested for:	Applied in	Strength	Weaknesses
DBI	$$DBI = \sum \frac{D}{\delta + D}$$ **D** = daily dose of an individual drug δ = minimum recommended daily dose of the individual drug $\sum$ = *indicates that the DBI is the sum score of prescribed drugs with probable anticholinergic and sedative properties for each patient* *Ex.* *A patient who takes 10mg Temazepam each night* *-minimum licensed dose on the US Food and Drug Administration label of 7.5mg* *Hence (10/10+7.5)=0.57* *DBI=0.57*	-anticholinergic -sedatives	-In performing the DBI calculation, each drug (ingredient) has a DBI SCORE *between 0 and 1*	**Univariate analysis** was undertaken to investigate potential risk factors for falling Negative Binomial Regression Models to give incidence rate ratio (IRR)- for the associations between DBI category and fall rate; between common drug classes and fall rate Probability of falling at 6 months was estimated as 1 minus the Kaplan-Meier estimate Analyses were performed using SAS 9.1 statistical software (SAS Institute, Inc., Cary, NC).	-community-dwelling population in US, Canada, Australia, New Zealand, UK and Europe -residential facilities -hospitals	-help clinicians recognize anticholinergic and sedative medicines that can impair function and prompt them to minimize their patient's exposure to these medicines -developed to estimate the risk of functional impairment from medications with the goal of becoming a clinical risk assessment tool -Electronic DBI calculators have been developed to inform clinicians of their patient's DBI and its associated risks	-limited to medications with anticholinergic and sedative effects -does not consider other medication classes that can cause adverse effects in older adults and does not provide specific clinical guidance -no published randomized controlled trials demonstrating the clinical efficacy and safety of using DBI as a clinical risk assessment tool.

STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drug

Title	Components	Medicines	Scoring	Tested for:	Applied in	Strength	Weakness
STOPPFall	Computerized Clinical Decision Support System Method: Deprescribing (Withdrawing medications among fallers)	-Benzodiazepines -Antidepressants -Antipsychotics -Antiepileptics -Diuretics -Centrally-acting Antihypertensives -Vasodilators used in cardiac diseases -Alpha-blocker antihypertensives -Alpha-blockers for Benign Prostate hyperplasia -Sedative Antihistamines -Medications for overactive bladder and urge incontinence	Instead of using a scoring system, a practical deprescribing tool was developed to aid in clinical decision-making.	In 2019, 24 panelists from 13 European nations completed each Delphi round questionnaire, and in 2020, 24 panelists completed the deprescribing tool questionnaire.	based on evidence from recent meta-analyses and national fall prevention guidelines in Europe	- STOPPFall was developed by two facilitators using data from recent meta-analyses and European national fall prevention standards. In three Delphi panel rounds, twenty-four panelists chose their level of agreement on a Likert scale with the STOPPFall items. -first European-wide effort to establish a consensus on FRIDs in older adults - When comparing the STOPPFall to national fall prevention guidelines, it is clear that it is more comprehensive than most guideline	-using this Computerized Clinical Decision System requires successful implementation through dissemination of the tool among healthcare professionals -panelists could not reach consensus on 17 medications classes regarding whether they should be classified as FRIDs **Delphi Process Limitations:** -the formulation of the questions by the facilitators might have influenced the responses, and individual panellists might have interpreted the

						listings (the STOPPFall includes items like alpha-blockers, centrally acting antihypertensives, antihistamines, and anticholinergics that aren't commonly included in guidelines). -panelists were asked to comment also based on their expertise in the field and clinical experience -deprescribing tool (using step wise approach) guide can help overcome current reluctance in clinical practice by providing an up-to-date and straightforward source of expert	questions somewhat differently, even though the purpose of the study was described in detail in the invitation letters -no face-to-face meetings were organised during the rounds due to lack of feasibility and inclusion of panellists from the whole continent -evidence given for panelists was based on heterogeneous observational studies that have typically quality issues such as accounting for confounding by indication -general standard of consensus measurement and an agreement concerning the declaration

						knowledge -- provides the decision maker with objective evidence to make a judgment	of consensus in Delphi studies do not exist to date, and various methods have been used - performing a time-consuming analysis adequately in a busy clinical environment is difficult - various factors - are involved in decision-making, and these cannot be accurately reflected in a decision tree.

Effectiveness of medication withdrawal in older fallers: results from the Improving Medication Prescribing to reduce Risk Of FALLs (IMPROveFALL) trial

Title	Components	Medicines	Scoring	Tested for:	Applied in	Strength	Weakness
No available tool but the objective of the study is to investigate the effect of withdrawal of fall-risk-increasing-drugs (FRIDs) versus 'care as usual' on reducing falls in community-dwelling older fallers	The use of fall-risk-increasing-drugs (FRIDs), including psychotropic and cardiovascular drugs	-Cardiovascular(Digitalis, antiarrhythmics, Nitrates, antihypertensives, diuretics, Beta-blockers, ACE/angiotensin inhibitors -Psychotropic FRIDs (Opioids, anti-epileptic, anti-parkinson, neuroleptics,anxiolytics, sedatives/hypnotics, antidepressants,anti-vertigo -Other FRIDs (anticholinergics, hypoglycemics, anti-spasmodics, alfa-blockers, steroids, NSAID, Anti-gout, Hydroquinine (muscle relaxant), Adrenergics, cough suprressants (Opiods), antihistamines	-None	-Data were analysed according to the intention-to-treat principle (primary) and pre-protocol (secondary) -Hazard ratios for falling were calculated using Cox-regression model	-612 older adults who visited an Emergency Department (ED) because of fall	-Patients meeting the following inclusion criteria were eligible for enrolment: aged ≥65 years community-dwelling - The follow-up period was 12 months	-In the current RCT, the single intervention of FRIDs withdrawal was not effective in reducing falls -Prescribing of the drugs, which involved a weighing of benefit and risk, both before the fall and in the represcribing over the subsequent year, was already fairly satisfactory. -In the intervention group, there was limited compliance, especially concerning psychotropic drugs withdrawal. - FRIDs-withdrawal is difficult to maintain over 1 year, in a population of complex, multimorbid older fallers. Compliance was difficult to maintain.

Synthesis of Results

Reference	Document Type	Tools Evaluated	Statistical Intervention	Results
Poe et al. (2018)	Review	JHFRAT	Sensitivity: 78%; 78.9%; 62% Specificity: 83%; 55.8%; 69.5% PPV: 30.8% NPV: 91.4% AUC: 0.708 Interrater reliability: 0.96	The JHFRAT is found to be reliable, having high sensitivity and negative predictive validity. The specificity and positive predictive validity of the results were both lower than expected.
Seppala et al. (2020)	Research paper	STOPPFall	Delphi Round questionnaire which completed by 24 panelists from 13 European countries (2019) and 24 panelists (2020)	The panelists agreed to include 14 drug classes in the STOPPFall. Psychotropic drugs were the majority of them. With relation to fall-risk-increasing features, the panelists identified 18 distinctions between pharmacological subclasses. For STOPPFall drug classes, practical deprescribing assistance was established.
Welch et al. (2016)	Evidenced-based report	FRAT	Sensitivity: >70% Specificity: >70%	The Fall Risk Assessment Tool met the specificity and sensitivity criteria of >70% and could be used for both screening and fall risk assessment.
Lohman et al. (2017)	CDC guideline report	STEADI	Sensitivity: 65% Specificity: 65%	The STEADI-Rx Algorithm outlines three steps that pharmacists can do to help their elderly patients avoid falling: screen, assess and coordinate care. Each step adheres to the Joint Commission of Pharmacy Practitioners (JCPP).

Cont.

Reference	Document Type	Tools Evaluated	Statistical Intervention	Results
Hendrich et al. (2020)	Research article	Hendrich II Fall Risk Model	Sensitivity: 78.72% Specificity: 64.07% AUC: 0.765	The overall rate of decline was 0.29 percent. There were 5, 492 falls and 76,800 non-falls recognized at the usual HIIFRM score level (fall rate 0.36 % ; HIIFRM specificity 64.07% , sensitivity 78.72%). The area under the receiver operating characteristic curve for the HIIFRM to predict falls was 0.765 (standard error 0.008; 95% confidence interval 0.748, 0.781;p 0.001), showing moderate accuracy.
Roza da Costa et al. (2012)	Systematic review Meta-analysis	Downton	Sensitivity: 92% Specificity: 36% PPV: 33% NPV: 93%	A single study found that the Downtown Fall Risk Index instrument has a high sensitivity of 92%. It does not, however, provide the optimal balance of sensitivity and specificity.
Blalock et al. (2020)	Research article	Drug Burden Index (DBI)	Interrater reliability: 1.90	DBI scores were higher in those who screened positive for fall risk (n = 1058) than in those who did not (Means = 0.98 (SD = 1.00) versus 0.59 (SD = 0.74), respectively, p 0.0001). Hence, DBI is a helpful technique that could be used to improve future research and practice by concentrating limited resources on people who are most at risk of medication-related falls.
Kouladjian et al. (2016)	Manuscript	Drug Burden Index Calculator	Sensitivity: 100%	The manual and the CCDSS application had a high level of agreement (Cohen's Kappa 0.95). The average time (mins:secSD) for participants to complete the task during the evaluation phase was 7:201:45, and 80 percent of pharmacists found the DBI Calculator effective in distinguishing sedative and anticholinergic medications in practice.

Cont.

Reference	Document Type	Tools Evaluated	Statistical Intervention	Results
Michalcova et al. (2020)	Research article	Inclusion of medication-related fall in FRAT (no tool produced)	High risk category A of active substances for increasing fall risk: 47% Fall experienced: n=188	Based on their adverse drug effect profile in SmPCs and frequency of usage in older patients who had undergone at least one documented fall in a geriatric care facility, it was able to construct a preliminary category of FRIDs. Despite the fact that more than half of the study participants had high fall risk scores upon admission, their fall risk may have been overestimated due to the widespread use of high fall risk medications, including simultaneous usage. More research is needed to refine the FRID classification and examine its effects on the risk of falling.
Rumuro and Vaiden (2012)	Review	Two Stage Model (FASPIP)- no tool produced		A complete list of drugs linked to falls has been compiled based on the available research. As new drugs are approved by the FDA or found as causing falls in the literature, this list will be updated. The list is intended to be used in conjunction with the updated MAI tool. The tool contains over-the-counter (OTC) and herbal products that have been documented in the literature. The list comprises the most often prescribed drugs that have been linked to falls in clinical practice.
Boyé et al. (2017)	Short report	IMPROveFall	Intervention to first fall: (HR 1.17;95%CI 0.89-1.54 Time to second fall: (1.19;0.78-1.82) Time to first fall-related GP-consultation: (0.66; 0.42-1.06) Time to first fall-related ED-visit: (0.85;0.43-1.68)	During the 12-month follow-up, 91 (34%) of control individuals and 115 (37%) of intervention participants encountered a fall; 35% of all attempted interventions failed, either due to recurrence of the initial indication for prescribing, extra medication for newly identified diseases, or non-compliance. The overall percentage of users of 3 FRIDs in the intervention and control groups did not change after 12 months when compared to baseline. Time to first fall (HR 1.17; 95 percent confidence interval 0.89–1.54), time to second fall (1.19; 0.78–1.82), time to first fall-related GP consultation (0.66; 0.42–1.06), or time to first fall-related ED visit (0.85; 0.43–1.68) were all unaffected by our intervention. Our single intervention of FRIDs withdrawal was ineffective in reducing falls in this cohort of complicated multimorbid individuals who visited an ED due to a fall.

Appendix 3
Dissemination of Research

Deprescribing Fall Risk-increasing Drugs in Older Patients

Authors: Fernandez VL, Gauci M, Azzopardi LM,

Institute: Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida, Malta

Background and Objective
Drug-related falls are of particular concern in older people since they lead to increased morbidity and mortality. The aim was to assess applicability and outcome of the application of fall medication risk assessment tools.

Setting and Method
The research was conducted in Karin Grech Hospital, a rehabilitation hospital. A literature review identified five multifactorial tools and three medication-based tools. The STOPPFall tool from the medication-based category was chosen. To assess the extent of deprescribing fall risk-increasing drugs (FRIDs), pharmacy profiles of patients aged 60 years and over admitted due to a fall with or without a fracture were retrospectively analysed during January to July 2021, and after intervention during October 2021 and January 2022. Clinical pharmacists were presented with the application of the STOPPFall tool to deprescribe FRIDs as an intervention to support deprescribing during medication management. T-test for one proportion and paired t-test were applied.

Main outcome measures
Deprescribing of fall risk-increasing drugs, assessment of effectiveness of intervention to empower pharmacists using STOPPFall tool

Results
In the pre-intervention study, the average age of the 55 patient profiles assessed was 81 years (65% females). Antidepressants (n=35), diuretics (n=34), opioids (n=31) and benzodiazepines (n=23) were the most frequently prescribed FRIDs. Significant deprescription rates were evident for opioids (97%, $p<0.01$) and benzodiazepines (70%, $p=0.030$). Diuretics (47%), antipsychotics (46%) and antidepressants (37%) showed lower deprescription rates.
The post-intervention study evaluated 58 patient profiles with an average age of 79 years (71% females). Diuretics (n=41), opioids (n=39) and antidepressants (n=26) were the most commonly prescribed FRIDs. Opioids (97%, $p<0.01$) and antipsychotics (67%, $p=0.027$) were significantly deprescribed. Results of pre and post analyses showed that the intervention did not significantly increase the deprescription of the FRIDs

Conclusion
The intervention to enhance application of the selected tool by clinical pharmacists did not significantly increase deprescribing of FRIDs.

Reference:
Seppala LJ, Petrovic M, Ryg J, Bahat G, Topinkova E, Szczerbinska K, et al. STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Age Ageing 2020;1-11.