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Title	Strategies to prevent potentially inappropriate prescribing and adverse drug reactions in older patients
Authors	Cullinan, Shane
Publication date	2015
Original Citation	Cullinan, S.P. 2015. Strategies to prevent potentially inappropriate prescribing and adverse drug reactions in older patients. PhD Thesis, University College Cork.
Type of publication	Doctoral thesis
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Download date	2026-11-16 09:54:00
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Strategies to Prevent Potentially Inappropriate Prescribing and Adverse Drug Reactions in Older Patients

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A thesis submitted to the National University of Ireland, Cork for the degree of Doctor of Philosophy in the School of Pharmacy

September 2015

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Declaration

I declare that the work contained within this thesis has not been previously submitted for a degree at this or any other university. All the work contained within this thesis is entirely my own work, apart from that indicated in the acknowledgements. I give my permission for the library to lend or copy this thesis upon request

Signed:_____ Date:_____

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Abbreviations

A+E	Accident and Emergency
ACE-I	Angiotensin Converting Enzyme Inhibitor
ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
AMTS	Abbreviated Mental Test Score
AOU	Assessment of underutilization of medication
BCT	Behavioural Change Therapies
CASP	Critical Appraisal Skills Programme
CDSS	Computerised Decision Support Systems
CGA	Comprehensive Geriatric Assessment
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CUH	Cork University Hospital
ENTREQ	Enhancing transparency in reporting the synthesis of qualitative research
FI	Frailty Index
FP7	European Commission Seventh Framework
FRAIL	Fatigue, Resistance, Ambulation, Illnesses, Loss of weight
GP	General Practitioner
HCP	Healthcare Professional
HSE	Health Service Executive
IPET	Improved Prescribing in the Elderly Tool
IT	Information Technology
MAI	Medication Appropriateness Index

MCQ	Multiple Choice Question
MDT	Multi-disciplinary Team
MMSE	Mini Mental State Examination
MUH	Mercy University Hospital
MUR	Medication Usage Review
NCHD	Non-Consultant Hospital Doctor
NHS	National Health Service
NORGEP	Norwegian General Practice Criteria
NSAID	Non-Steroidal Anti-inflammatory Drug
OECD	Organisation for Economic Co-operation and Development
OPERAM	Optimising Therapy to prevent avoidable hospital admissions in the Multimorbid elderly
OR	Odds Ratio
OTC	Over the Counter
PAI	Prescribing Appropriateness Index
PIM	Potentially Inappropriate Medication
PIP	Potentially Inappropriate Prescribing
PPO	Potential Prescribing Omissions
PROTECT	Prescribing Outcomes for Trainee doctors Engaged in Clinical Training
RCT	Randomised Controlled Trial
SD	Standard Deviation
SENATOR	Development and clinical trials of a new Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons
SHARE	Survey of Health, Ageing and Retirement in Europ
SHiM	Structured History Taking of Medication Use

SHO	Senior House Officer
SPSS	Statistical Package for the Social Sciences
START	Screening Tool to Alert Doctors to Right Treatment
STOPP	Screening Tool of Older Persons Potentially Inappropriate Prescriptions
TCA	Tricyclic Antidepressants
TDF	Theoretical Domains Framework
UCC	University College Cork
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

Publications

Peer-reviewed publications

- **Cullinan S**, O'Mahony D, Byrne S. Use of a frailty index to identify potentially inappropriate prescribing and adverse drug reaction risks in older patients. *Age and Ageing (In press)*

- **Cullinan S**, Fleming A, O' Mahony D, Ryan C, O' Sullivan D, Gallagher P, Byrne S. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalised patients: A qualitative study. *British Journal of Clinical Pharmacology (November 2014)*

- **Cullinan S**, O' Mahony D, Fleming A, Byrne S. A meta-synthesis of potentially inappropriate prescribing in older patients. *Drugs and Aging (June 2014)*

- Fleming A, Bradley C, **Cullinan S**, Byrne S. Antibiotic prescribing in long-term care facilities: A meta-synthesis of qualitative research. *Drugs and Aging (April 2015)*

- Fleming A, Bradley C, **Cullinan S**, Byrne S. Antibiotic prescribing in long-term care facilities, a qualitative, multidisciplinary investigation. *British Medical Journal Open (November 2014)*

- Almarsdottir A B, **Cullinan S**, Masdottir B B, Byrne S. Pharmacist expertise in designing a decision support tool for optimisation of drug therapy in older persons. *Research in Social and Administrative Pharmacy (September 2014)*

- O' Sullivan D, O' Mahony D, O' Connor M N, Gallagher P, **Cullinan S**, Gallagher J, Eustace J, Byrne S. The impact of a structured pharmacist intervention on the appropriateness of prescribing in older hospitalized patients. *Drugs and Aging (May 2014)*

Papers under review in peer-reviewed journals

- **Cullinan S**, O' Mahony D, Byrne S. Use of an e-learning educational module to better equip doctors to prescribe for older patients - A randomised controlled trial (British Journal of Clinical Pharmacology)

- **Cullinan S**, O' Mahony D, Byrne S. Could the Structured HIstory taking of Medication use (SHiM) tool optimise prescribing for older patients and reduce adverse events? (International Journal of Clinical Pharmacy)

Peer-reviewed published abstracts

- **Cullinan S**, O' Mahony D, O' Sullivan D, Byrne S. Use of a frailty index to identify instances of potentially inappropriate prescribing. *Pharmacoepidemiology and Drug Safety (June 2015)*

- Fleming A, Bradley C, **Cullinan S**, Byrne S. A multidisciplinary, qualitative study investigating the factors influencing antibiotic prescribing in long-term care facilities in Ireland. *International Journal of Pharmacy Practice 2014*

- **Cullinan S**, Fleming A, O' Mahony D, Ryan C, O' Sullivan D, Gallagher P, Byrne S. Why? A qualitative study of potentially inappropriate prescribing in older patients. *International Journal of Clinical Pharmacy (October 2013)*

- **Cullinan S**, O' Mahony D, Fleming A, Byrne S. Potentially inappropriate prescribing in older patients: A meta-synthesis. *International Journal of Clinical Pharmacy (October 2013)*

Book chapters

- Taxis K, O' Sullivan D, **Cullinan S**, Byrne S. Drug utilisation in older people. Drug Utilisation Research (Wiley publishing). Due for publication September 2015.

Posters and presentations

- **Cullinan S**, Fleming A, O' Mahony D, Ryan C, O' Sullivan D, Gallagher P, Byrne S. Why? A qualitative study of potentially inappropriate prescribing in older patients-Interim analysis. All Ireland Schools Pharmacy Conference 25th and 26th March 2013, Belfast, Northern Ireland - Poster

- **Cullinan S**, Fleming A, O' Mahony D, Ryan C, O' Sullivan D, Gallagher P, Byrne S. Why? A qualitative study of potentially inappropriate prescribing in older patients. European Society of Clinical Pharmacy (ESCP) Conference 16th – 18th October 2013, Prague, Czech Republic - Poster

- **Cullinan S**, O' Mahony D, Fleming A, Byrne S. Potentially inappropriate prescribing in older patients: A meta-synthesis. European Society of Clinical Pharmacy (ESCP) Conference 16th – 18th October 2013, Prague, Czech Republic – Poster

- **Cullinan S**, Fleming A, O' Mahony D, Ryan C, O' Sullivan D, Gallagher P, Byrne S. Why? A qualitative study of potentially inappropriate prescribing in older patients. European Society of Clinical Pharmacy (ESCP) Conference 16th – 18th October 2013, Prague, Czech Republic – Oral presentation

- **Cullinan S**, Fleming A, O' Mahony D, Ryan C, O' Sullivan D, Gallagher P, Byrne S. Potentially inappropriate prescribing in older patients: causes and solutions. School of Pharmacy Seminar Series 1st May 2014, University College Cork, Ireland – Oral presentation

- **Cullinan S,** Byrne S, Masdottir B B, Almarsdottir A B. Development of a pan-European drug file for incorporation into a computerised decision support system. Drug Utilisation Research (EuroDURG) Scientific Meeting 27th-29th August 2014, Groningen, The Netherlands – Poster

- **Cullinan S**, O' Mahony D, O' Sullivan D, Byrne S. Use of a frailty index to identify instances of potentially inappropriate prescribing. Prescribing and Research in Medicines Management (PRIMM) Conference 23rd January 2015, London, United Kingdom – Oral presentation

- **Cullinan S,** Byrne S. STOPP/START version 2, considerations for implementation. NHS Medication Use and Safety Network meeting 25th June 2015, London, United Kingdom – Oral presentation

Postgraduate taught module credits awarded

- PG6009 – Graduate Information Literacy Skills

  Credit weighting: 5

- PG6001 - Scientific Training for Enhanced Postgraduate Study (STEPS)

  Credit weighting – 5

- PG7016 - Systemic reviews for the health sciences

  Credit weighting - 5

Thesis Abstract

Introduction

Potentially inappropriate prescribing (PIP) is an umbrella term which encompasses prescribing of medications:

(i) With no indication

(ii) For the wrong indication

(iii) With a high risk of an adverse drug event (ADE)

(iv) That are unnecessarily expensive

(v) For too short or too long a period.

PIP also includes the failure to prescribe appropriate drug therapy when it may be of benefit to the patient. PIP is a major contributor to ADEs, adverse drug reactions (ADRs), hospitalisations, patient harm and overall increased healthcare costs. Older patients are particularly susceptible to PIP due to multiple comorbidities, multiple medications and declining renal and hepatic function leading to altered pharmacodynamic and pharmacokinetic properties of drugs. Rates of PIP in primary, secondary and long-term care as high as 40%, 58% and 70% respectively have been reported. ADRs, one of the more serious consequences of PIP, are in their own right, a major contributor to hospitalisations and increase costs, especially amongst the older population. Patients over 65 years of age are estimated to be 4 times more likely to experience an ADR than their younger counterparts. While much quantitative research has taken place to quantify the problem of PIP, little in the way of qualitative research exists to identify the

fundamental causes of this phenomenon. As a result, interventions aimed at addressing PIP have had only modest success.

The overall aim of this thesis was to identify , develop and implement strategies with the potential to prevent PIP and ADRs in older patients.

The objectives were:

(i) to explore the causative factors of PIP and related outcomes through qualitative research

(ii) use these findings to determine the types of interventions that would be suitable for the purpose of preventing PIP

(iii) develop an intervention informed by this research

(iv) explore other possible intervention types identified for suitability and applicability with regards to preventing PIP and related outcomes.

Methods

Since this work was to be informed by qualitative research, a systematic review of the qualitative literature on PIP was undertaken to determine what work had already been done, and to create a context in which later research could be compared. The meta-synthesis was conducted using the meta-ethnographic approach developed by Noblit and Hare. The ENTREQ (Enhancing transparency in reporting the synthesis of qualitative research) statement, a framework for reporting the synthesis of qualitative health research, was used to guide how the results were reported, as well as the PRISMA checklist.

An empirical qualitative study was then carried out in four hospitals in the Munster region of Ireland. Semi-structured interviews were used to explore doctors' perspectives on the barriers to appropriate prescribing in older hospitalised patients. To identify possible areas of intervention, the theoretical domains framework (TDF), an overarching theoretical framework combining 128 constructs from 33 theories of behaviour change was used to analyse the data. The TDF consists of 12 'theoretical domains'. The domains identified in the TDF were then mapped to the behavior change wheel to identify suitable intervention types.

One of the intervention types identified was 'training'. Therefore, for the next stage of the work, a randomised controlled trial (RCT) was developed to assess the impact of an online educational module on doctors' knowledge and confidence with regards to prescribing for older patients. Doctors in both control and intervention groups completed assessment at baseline. Similar assessments were then completed 4 weeks post intervention and again at 12 weeks.

Other suitable intervention types identified by the previous qualitative work included 'enablement' and 'environmental restructuring'. Therefore, the next stage of the work involved exploring the potential for a frailty index score as a means of altering doctors' working *environments* in such a way as to *enable* them to readily identify patients at increased risk of PIP and ADRs. A frailty index was developed and applied retrospectively to a database of 711 patients. The relationship between patients' frailty index scores, appropriateness of prescribing and likelihood of experiencing an ADR was explored. This was followed by another prospective observational study, testing these findings in another patient group.

Finally, and again, targeting 'enablement' as a suitable intervention type, the potential for the Structured HIstory taking of Medication use (SHiM) tool to *enable* doctors to optimise prescribing for older patients and reduce adverse events was explored. SHiM was applied to 123 hospitalised patients in a prospective observational study. Whether or not the findings from SHiM would optimise prescribing and reduce clinically significant adverse events was explored.

Results

The meta-synthesis returned 7 relevant papers, highlighting the lack of qualitative work published in the area of PIP. Four key concepts emerged from the 7 papers as being contributory factors to PIP:

(i) Desire to please the patient

(ii) Feeling of being forced to prescribe

(iii) Tension between experience and guidelines

(iv) Prescriber fear.

Ultimately it was shown that in many situations, prescribers suffer from 'self-perceived restrictions' leading to a sense of powerlessness to prescribe appropriately for older patients. This forces prescribers to rely on what they know and have done before, which leads to the PIP that has been identified in previous quantitative studies.

Four over-arching themes also emerged from the empirical qualitative study as being contributory to PIP. They were;

(i) Lack of education in the area of geriatric pharmacotherapy

(ii) prescribing environment that is conducive to PIP

(iii) Poor information technology (IT) infrastructure

(iv) Lack of collaboration between the various levels of patient care.

5 domains within the TDF were found to be relevant:

(i) Environmental context and resources

(ii) Memory/attention and decision processes

(iii) Knowledge

(iv) Skills

(v) Social influences.

When these were mapped to the behavior change wheel, the intervention types deemed suitable to address PIP were training, environmental restructuring, restrictions, persuasion, incentivisation, modelling and enablement.

In the RCT, the online educational module resulted in a highly significant 22% difference in test scores between intervention and control groups 4 weeks post-intervention. This improvement was maintained at 12 weeks. The module also improved doctors' confidence levels with regards to prescribing for older patients. The study reinforced findings from the qualitative research that doctors do not receive enough specific geriatric pharmacotherapy training as undergraduates.

The two studies exploring the use of a frailty index score as an indicator of patients at increased risk of PIP/ADRs showed that there is a significant positive relationship between a patient's frailty status and their likelihood of experiencing PIP/ADRs. A

frailty index threshold of 0.16 was identified; patients above this threshold were at least twice as likely to experience PIP/ADRs.

SHiM was found to be a useful tool in terms of reconciling patients' medications. However, the evidence for it being capable of preventing clinically relevant adverse events was poor. While SHiM uncovered 200 discrepancies between the medication list obtained by the physician and what the patient was actually taking at home, only 1% of adverse events experienced by patients during their hospital stay would have been prevented by application of SHiM.

Conclusion

Qualitative research in this thesis has proposed novel theories relating to the causative factors of PIP in older patients. In doing so, it has identified several areas for intervention and laid down a road map for future research. This work has also shown that relatively simple educational interventions are vital for equipping doctors to prescribe appropriately for older patients. It has also illustrated the potential benefit of interventions based on providing doctors with simple but relevant indicators which might identify patients at risk of PIP/ADRs.

Acknowledgements

- Firstly, I would sincerely like to thank both my PhD supervisors Prof. Stephen Byrne and Prof. Denis O' Mahony, for their continued support, generosity of time, encouragement and guidance. Their dedication, expertise, and hard work have been invaluable to the completion of this thesis.

- I would like to thank my friends from the clinical pharmacy research office; Kevin Murphy, James Gallagher, Aoife Fleming, David O' Riordan, Kieran Walsh, Maria Kelly, Aoife McGillicuddy and Michael McCarthy for their help and encouragement over the last few years. I would especially like to thank Dr. David O'Sullivan and Dr. Cristin Ryan for all their help at the beginning of my PhD and throughout, it is greatly appreciated.

- I would like to thank the staff in the School of Pharmacy, especially Aisha Murphy and Kathleen Williamson for always being so accommodating and so helpful.

- I would like to thank the staff of Cork University Hospital, particularly everyone in Accident and Emergency who were so helpful and willing when it came to research. Special thanks to Dr. Amanda Lavan for her assistance, and insights.

- I would like to thank all involved in the SENATOR project. Special mention to Mary-Claire O' Regan and Niamh Quann for their help and understanding over the years, especially during the writing of this thesis.

- I would like to thank my family, especially my mother and father, who have always encouraged and supported me and been there for me in any way that was ever required.

- Finally, I would like to thank my fiancée Marion for her continual support, understanding and patience, without which this would not have been possible.

1. Thesis introduction

1.1 The ageing population

Within the 34 member countries of the Organisation for Economic Co-operation and Development (OECD), people born today have an average life expectancy of 80.1 years [1]. This is a 10 year increase from just 45 years ago. Sixty-five year olds today have an average life expectancy of 19.25 years, almost a 6 year increase from 1960. Of these extra 19 years, 9 are likely to be 'healthy years' [2]. In 1960, 8.6% of the OECD population was aged 65 or older. Today, that figure is 15.4% and set to rise to 27.2% by 2050 [3, 4]. These statistics clearly illustrate that our population is ageing. With an ageing population come many socioeconomic burdens and increased pressures at all levels of care.

In primary care, General Practitioners (GPs) care for more and more patients over the age of 65. Escalating time pressures, coupled with a rising workload and intense scrutiny older patients' treatment regimens demand, have resulted in many GPs feeling overwhelmed and incapable of providing the level of care required for older patients [5, 6]. In secondary care in 2011, 43% of total hospital inpatient expenditure in the OECD countries was on patients over 65 years of age [7]. We are also seeing a reduction in available hospital beds with figures dropping from 7.2 per 1,000 population in 2000, to 5.9 per 1,000 in 2010 [8]. In the long term care sector there has been 4% growth in expenditure on institutional care since 2000, which aligns with the 5% growth in the number of long term care patients over the age of 65 since 2000 [9]. These figures paint a picture of increasingly stressed health care systems pushed to breaking point by the ageing population, and are as much a representation of the Irish healthcare system as they are the global picture.

Figure 1.1 illustrates how the world's population is changing and is set to change in the future.

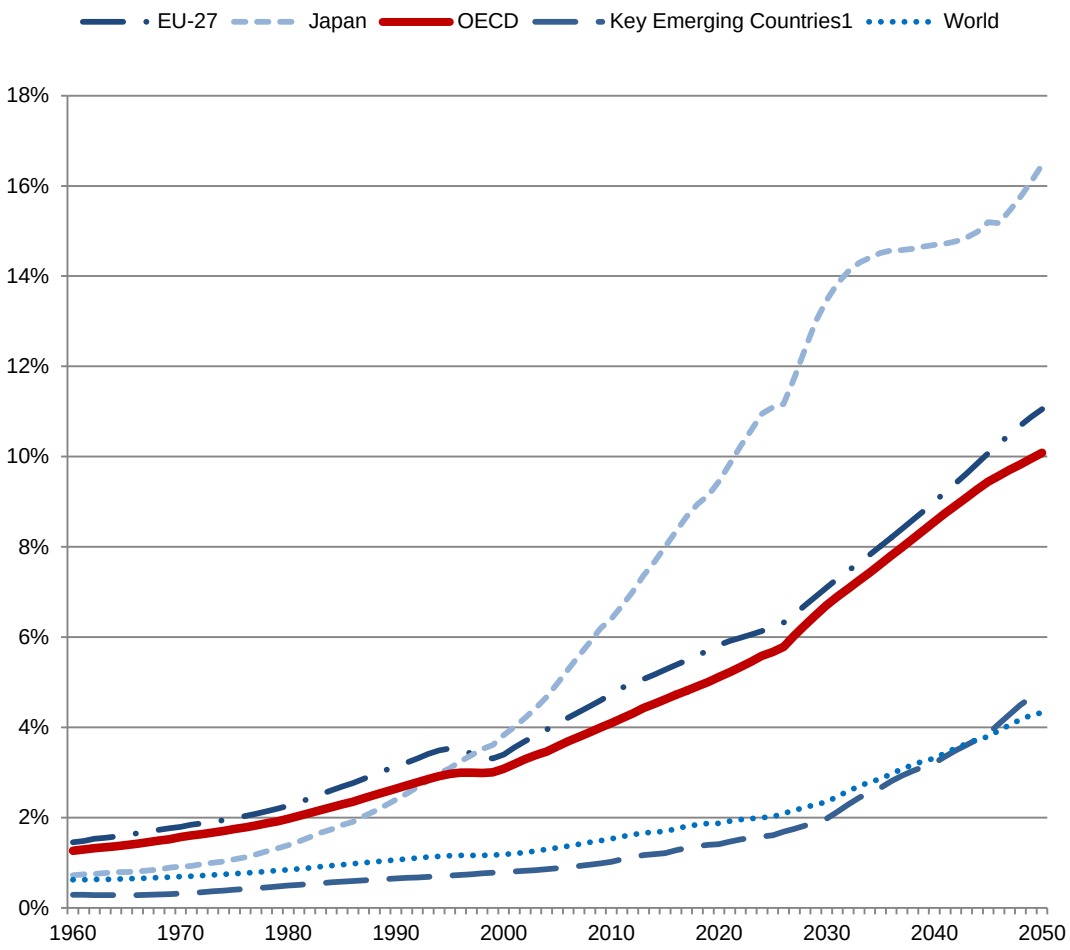


Figure 1.1 Trends in the share of the population aged over 80 years, 1960-2050 [10]

It is not *just* the number of older patients that is the problem. The complexity and potential adversity of their healthcare management also places a strain on both healthcare professionals and the State alike. Older patients, particularly those aged over 80 years, commonly suffer from multiple co-morbidities and consequently, take multiple medications. Recent studies investigating medication usage in Irish

patients over 65 have reported average number of regular medications to be between 5 and 8 per patient [11-14]. Physiological, age-related changes commonly result in altered pharmacokinetic and pharmacodynamic properties of these medications. Consequently, older patients are a vulnerable demographic group in terms of drug-drug interactions, drug-disease interactions, potentially inappropriate prescribing (PIP) and adverse drug reactions (ADRs).

1.2 Potentially inappropriate prescribing (PIP)

PIP is a term used to describe a range of sub-optimal prescribing practices and is particularly prevalent amongst the older population. In essence, it includes;

(i) the prescribing of potentially inappropriate medications (PIMs) that carry an unacceptable risk of ADR when a safer alternative is available

(ii) the prescribing of medications at a dose or duration unsuitable for older patients and

(iii) the under-prescribing of medications which may benefit an older patient. These latter cases are commonly referred to as potential prescribing omissions (PPOs) [15, 16].

PIP prevalence rates of 21%, 51% and 70% in primary, secondary and long-term care respectively have been reported in Ireland alone [11, 13, 17]. Further afield, PIP prevalence studies have shown rates amongst older patients to be high also e.g. USA (42%), Asia (40.4%), Australia (32.3%), Europe (30.4%), South America (28%) and Canada (16.3%) [11, 18-22]. PIP has been well established as a major

contributory factor to hospitalisations, ADRs and increased costs [11, 23-27]. In 2010, Cahir *et al.* performed a cost analysis of PIP in Ireland. They reported that in one year, the total cost of PIP in terms of medication costs was €45 million, which equated to 9% of the overall expenditure on pharmaceuticals in those aged 70 years and over [28]. This doesn't take into account other costs associated with PIP such as increased length of hospital stays or hospitalisations due to ADRs.

One of the most serious consequences of PIP is the occurrence of ADRs. An ADR is defined as *"any response to a medicine that is noxious or unintended attributable to a medicine, which occurs at a dose which is normally for use in human beings, for the purpose of prophylaxis, diagnosis, therapy or modification of a physiological function"* [29, 30]. An adverse drug event (ADE), refers to "*any injury occurring at the time a drug is used, whether or not it is identified as a cause of the injury*" [29]. An ADR is a special type of ADE in which a causative relationship can be readily shown. ADRs have been reported to be between the 4th and 6th leading cause of death in hospitalised patients in the US [31]. Older patients in particular are 4 times more likely to experiences an ADR than the general adult population [32-34]. Historically, there has been some uncertainty as to whether or not PIP is a contributory factor to ADR occurrence [24, 35-39]. However, in more recent studies a clear relationship between the two has been identified [40-42]. It has been reported that ADR rates in patients seen at admission are as high as 35% [43], while 46% of inpatients experience an ADR [31]. 46% of older inpatients also experience ADRs [44]. As well as being a significant causative factor of hospital admissions [45-

48], ADRs are a major cause of increased health-care utilisation [23] through increased lengths of stay and increased costs. ADRs have been shown to result in an average of 2 additional days in hospital [49]. Davies *et al.* reported that in the UK, inpatient ADRs resulted in an extra 2000 bed days per annum [49], which equated to a cost of £171 million. This figure rises to £1 billion when all ADRs are accounted for [50]. Considering that 57% of ADRs are thought to be avoidable, ADRs represent a major healthcare problem that, for the most-part, could possibly be prevented [51].

1.3 Older patients susceptibility to PIP

As mentioned earlier, older patients are particularly vulnerable to PIP and associated outcomes such as ADRs. With an increasing burden of co-morbidities as patients' age, prescribers find themselves under increasing pressure to prescribe multiple medications. Best practice dictates that any decision a prescriber makes with regards to commencing a medication for a patient, should be evidence-based and the indication for which the drug is being prescribed is well established through evidence based on randomised controlled trials (RCTs). The difficulty when prescribing for older patients however, is that they are often excluded from such trials due to their often complex health status and multiple morbidities [52]. Therefore the situation arises where a clinician must prescribe without the evidence base he/she might have for someone in the younger adult population.

In addition to this, with ageing comes declining renal function and liver function, volume of distribution of lipid-soluble drugs increase, and sensitivity to several classes of drugs is often altered. These age-related pharmacokinetic and pharmacodynamics changes mean that older patients experience increased inter-individual variability with regards to how they metabolise drugs and how drugs affect them physiologically [53].

These age-related pharmacokinetic and pharmacodynamic changes affect drugs which are common treatments for co-morbidities often seen in older patients. For example, digoxin is a commonly prescribed treatment for congestive heart failure. However, in older patients, the time taken to reach steady-state plasma concentrations increases from 7 days (in a younger adult) to 12 days [54]. Volume of distribution is reduced in older patients, therefore requiring a reduction in loading dose in older patients, and because it is predominantly cleared through the kidneys, the overall daily dose often needs to be reduced in older patients due to their age-related decline in renal function [53-55]. Similarly, plasma concentrations of angiotensin converting enzyme (ACE) inhibitors are increased in older patients with reduced renal function thereby often necessitating a reduction in dose [56, 57]. Older patients are particularly vulnerable to adverse effects from neuroleptic medications. Delirium, extrapyramidal symptoms, arrhythmias, and postural hypotension are all side effects which are more prevalent in older patients due to altered pharmacokinetics and pharmacodynamics [58, 59] as well as increased sedation at lower doses of benzodiazepines [60-62].

These age-related changes, coupled with lack of evidence for the use of many drugs in older patients render these patients significantly more susceptible to PIP and PIP-related adverse outcomes than their younger counterparts. While most prescribers are of course well aware of the prescribing complexities of older patients, it is the variation between patients that often causes problems. The unpredictability of how drugs will affect any particular patient, or how an older patient will respond to a drug often presents a challenge to the prescrier in terms of prescribing the right medication at the right dose [53].

1.4 Interventions to address PIP and ADRs

Given the issues of greater levels of multi-morbidity and complex polypharmacy in an ageing global population, it is not surprising that PIP and ADR detection and reduction has been the focus of several intervention studies [14, 16, 52]. However, to date, little progress has been made in achieving significant improvements in appropriateness of prescribing in older patients on a global scale. The main strategies employed to address PIP and it's outcomes are detailed in the following section.

1.4.1 Methods of detection

In order to significantly reduce PIP and PIP related outcomes, robust methods of PIP detection must be applied. Historically, there have been several attempts to develop validated criteria to identify PIP. However, lack of transferability and validation by randomised controlled trials (RCTs) means that much of these efforts have not had the kind of effect that is required [52].

Criteria fall into two categories; explicit and implicit. Explicit criteria usually consist of a list of drugs, drug classes and doses which have been reported in the literature, or agreed upon by consensus methods to be potentially inappropriate in older patients. Implicit criteria are far more judgment based and rely more on the prescriber's knowledge. They are time-consuming and rather tedious to use, however they do focus more on the patient and address their drug therapy at a more individual level [52].

The first explicit tool for identifying PIP was Beers' criteria, published in 1991 [63]. Originally designed for use in nursing homes, the criteria consisted of a list of 30 drugs which were either to be completely avoided or avoided at certain doses/durations. Beers' criteria were updated three times in 1997, 2003 and 2012[64-66], and now consist of 53 medications divided into three categories:

(i) Medications to be avoided in older patients-independent of diagnoses or conditions

(ii) Medications to be avoided in older patients due to drug-disease interactions

(iii) Drugs to be used with caution in older patients.

They are widely utilised in the US and have also been applied in several European studies. In Ireland, a study using the Beers' criteria reported PIP prevalence of 32% in secondary care [36] while rates of 20%, 66% and 40% in primary, secondary and long-term care have been reported in other European sites [48, 67, 68]. However, Beers' criteria have several important limitations. They are very much focused on the US prescriber. Many of the drugs included are not available in Europe. Several

are not commonly prescribed for older patients and there is much disagreement surrounding the identification of some of the medications as drugs which should be avoided in *all* situations [52]. Drug-drug interactions, prescribing of two drugs from the same pharmacological class and PPOs are not accounted for. Considering that there have not been any RCTs assessing Beer's criteria's capacity to improve outcomes such as ADRs and hospitalisations, consequently, they have not found their way into common clinical usage.

Given the short-comings of Beers' criteria, O' Mahony *et al.* devised new PIP criteria. Following validation by Delphi consensus methods, the STOPP/START criteria were published in 2008 [69] and updated in 2014 [70]. The latest iteration of Screening Tool of Older Persons' Prescriptions (**STOPP**) consists of 87 prescribing scenarios, categorised by disease area, which are potentially inappropriate in older patients, and include common drug-drug and drug-disease interactions. The Screening Tool to Alert doctors to Right Treatment (**START**) consists of 34 prescribing scenarios, categorised by physiological systems, where certain medications should be considered for an older patient. STOPP/START has been extensively researched in several countries in 5 continents and has shown good inter-rater reliability between physicians and pharmacists [11, 71-73]. Studies have explored the use of the criteria in all levels of care [13, 17, 36] and have shown implementation of the guidelines to result in sustained improvement in medication appropriateness and superior performance in terms of PIP detection and ADR prevention when compared to Beers' criteria [16, 24]. STOPP/START has established itself as the principle tool in PIP detection, certainly outside of the US, but to

maintain its clinical relevance, the criteria will require regular up-dating and validation.

Other explicit tools have been developed around the world including: the Improved Prescribing in the Elderly Tool (IPET) [74], the Prescribing Appropriateness Index (PAI) [75], Zhan's Criteria [76], the French Consensus Panel List [77], the Australian Prescribing Indicators Tool [78], the Norwegian General Practice Criteria (NORGEP) [79], the PRISCUS List [80], the Thailand criteria [81] and the Rancourt criteria [82]. A recent review has highlighted the pros and cons of these various tools [52]. Lack of under-prescribing criteria, lack of availability of drugs outside the country of origin, lack of studies outside the country of origin, lack of drug-drug interaction data and lack of transferability are common drawbacks for most of these explicit criteria sets.

Unlike the explicit criteria described above, implicit prescribing criteria are not focused on particular drugs or disease areas. They consist of quality indicators of prescribing that a prescriber or pharmacist must use their own judgment to apply to a person's prescription. The most commonly utilised and cited of these is the Medication Appropriateness Index (MAI) [83]. The MAI consists of ten criteria which must be applied to each medication on a patient's prescription. The MAI poses questions like: "*Is this medication effective for the condition*?"; "*Are the directions practical*?"; "*Is the duration of therapy acceptable*?". Medications are rated according to each of the criteria and the sum of all the ratings provides a measurement of the overall appropriateness of that drug. This process is then repeated for each drug. The MAI has been extensively used in research to assess

prescribing appropriateness as an outcome in many studies [41, 84-86]. These studies have shown that the MAI tool has good inter-rater reliability amongst pharmacists and doctors and performs better than Beers' criteria with regards to predicting adverse drug events [41]. However, it is generally regarded as a laborious, time-consuming tool and does not account for under-prescribing. The Assessment of underutilization of medication (AOU) tool [87] however, solely identifies prescribing omissions. Again, the AOU tool has shown good inter-rater reliability but with more robust tools available now, particularly those which can identify both inappropriate prescribing and under-prescribing, the AOU is not commonly reported in the literature.

1.4.2 Comprehensive geriatric assessment

Considering the complexity of older patients' prescriptions, as well as the fact that they may well be under the care of multiple healthcare professionals due to the presence of multiple co-morbidities, it would seem logical that the care of an older patient should be overseen by a team of multiple healthcare professionals with different areas of expertise. The Multidisciplinary Team (MDT) approach involves a group of healthcare professionals working together to assess older patients' treatment plans including their medication regimen. In this way, the knowledge and expertise of each of the members of the MDT team is channelled in order to improve the overall quality of patient care, improve appropriateness of prescribing and minimise ADRs [35, 88].

In terms of older patients, an MDT will usually comprise a geriatrician working with a number of other specialist healthcare professionals (HCPs) from different aspects of geriatric medicine, i.e. nurses, physiotherapists, occupational therapists and pharmacists enabling them to perform a comprehensive geriatric assessment (CGA). The purpose of a CGA is not simply to examine a patient's prescription. The MDT takes a holistic approach to the care of older patients and their therapies, looking at all aspects, as well as their medications [89]. For example, a patient's cognitive and functional capacities will be assessed when making decisions about their future care and formulating a treatment plan. This type of approach addresses one of the key areas which render older patients vulnerable to PIP and PIP related outcomes i.e. complexity of care. Typically, older patients take multiple medications, often prescribed by multiple doctors, for multiple diseases. Without an appropriately trained and experienced person overseeing the therapy as a whole, it is highly likely that some degree of PIP will be present. A CGA performed by an MDT therefore is undoubtedly beneficial to older patients and doctors alike [89-91].

Several RCTs have shown that CGA improves prescribing appropriateness [89, 90, 92]. Schmader *et al.* reported reductions in potentially inappropriate medications (PIMs) as well as PPOs resulting from CGA [90]. Similarly, Saltvedt *et al.* showed a reduction in drug-drug interactions and in prescribing of drugs with high ADR risk in older patients receiving CGA [93]. These results are not surprising given the detailed nature of CGA. However, this approach is again time-consuming and staff-intensive.

Although, CGAs are not standard practice globally, nevertheless where CGA is in common practice it has been shown to be a powerful tool in not only improving prescribing appropriateness but also positively influencing other key clinical outcomes. This is the case in Belgium for example, where every hospitalised patient over 65 years of age undergoes CGA. A recent Belgian study illustrated the value of CGA in identifying patients at risk of hospital readmission post discharge [94].

1.4.3 Expert pharmacist review

With their expertise in medicines and medicines management, pharmacists are a logical choice when looking for health care professionals to reduce PIP and ADRs. An expert pharmacist review involves the pharmacist applying a standardised assessment to older patients' prescriptions and liaising with the prescribers to optimise the prescription. Generally, this is mainly available in hospital settings although community-based models do exist also. Pharmacists have been the focus of several initiatives aiming to improve prescribing appropriateness in the past e.g.

(i) Medications review

(ii) Participation in MDTs

(iii) Participation in ward rounds

(iv) Provision of patient counselling

(v) Delivery of educational sessions to both the patients and the prescriber [88, 95-100].

Such interventions have been proven to be effective at improving prescribing appropriateness in older hospitalised patients [14, 96].

A number of RCTs have illustrated the benefit of expert pharmacist led assessments [89, 95, 96, 98, 101]. Hanlon *et al.* reported a 24% decrease in MAI scores after three months in the intervention group. Not only was this maintained at twelve months but actually improved further to 28% [98]. Crotty *et al*. also showed an improvement in MAI scores [101] as did Spinewine *et al [95]* arising from expert pharmacist review. However no studies were able to show a significant difference in ADEs, falls, behaviour or cognition. Like CGA, expert pharmacist review is clearly of benefit, but is costly and resource intensive and is therefore a luxury rather than standard clinical practice. Also, there are no published RCTs reporting a clear link between expert pharmacist review and improved outcomes such as reduced incidence rates of ADEs. However, a recent RCT has shown that an expert pharmacist review in acutely ill older people significantly reduces incident ADR rates in hospital (20.9% event rate in control group versus 13.9% in intervention group) giving a relative ADR risk reduction of 33.3% [102]. This study incorporated pharmacist review with CGA and computerised decision supports systems (CDSS) which are described in more detail later in this chapter.

Medication usage reviews (MURs) are another obvious role for pharmacists in medication optimisation in older people. However, while certainly useful in settings where there may be a pharmacist trained in geriatric pharmacotherapy, MURs are not particularly helpful in everyday practice. This is because not all pharmacists are trained in geriatric pharmacotherapy and MURs may not be standardised or regulated such that there is much inconsistency with regards to information gleaned in an MUR and results achieved. Furthermore, there is no evidence that

MURs, whether standardised or not, actually improve prescribing appropriateness or reduce ADEs [52].

1.4.4 Prescriber education

If there is to be improved prescribing for older patients, then constant and up to date education of prescribers will always be paramount. It is not surprising therefore that educational interventions are one of the more common methods employed to improve prescribing appropriateness [103-105]. There are a number of different approaches to be considered when designing an educational intervention. Firstly, there is the traditional lecture based educational session and the related printed material disseminated to participants. Alternatively, there are more interactive interventions which involve participation and direct feedback. A number of studies have shown the latter to be more effective [106-108]. It is interesting to note that of the interventions described in the literature to date, few of the authors have elaborated on the reasons for choosing the type of intervention they chose. It is also interesting to note that while most report positive results, the evidence to-date relating to their overall effectiveness is mixed [99, 107-117].

To date, almost all of the educational interventions aiming to improve prescribing appropriateness in older patients have only been concerned with one drug or drug class. For example, Eide *et al.* explored the effect of pharmacist-led educational meetings with clinicians on the frequency and appropriateness of hypnotic medicines prescribed for older patients [117]. Fossey *et al.* used a similar approach to reduce the number of hypnotics prescribed [114]. Stein *et al.* used 30 minute

educational sessions to reduce the volume of NSAIDs prescribed for more than seven days in older patients [108]. Very few educational interventions address prescribing in general. While focusing all attention on one drug class does certainly benefit prescribers and their knowledge of that medicine, studies such as these are misplaced if what is required is *general* geriatric pharmacotherapy training.

1.4.5 Computerised decision-support systems

Computerised decision-support systems (CDSS) are computer applications designed to aid clinicians in making diagnostic and therapeutic decisions in patient care. The potential for such systems is considerable with respect to optimising prescribing in older patients. Unfortunately, Ireland is poorly developed compared to several European countries and North America in terms of healthcare information technology. The great majority of patient records in Ireland are still paper based. The tragedy in this is that the tools outlined above to detect PIP such as the STOPP/START criteria, are now starting to be coded and formatted in such a way that they could be implemented electronically as a CDSS [118].To do this however, they need to be able to link to the patient records electronically, which cannot currently be done in most sites in Ireland. In other countries however where this is possible, studies have shown just how effective CDSS can be, showing reductions in potentially inappropriate medications (PIMs), improvements in doses and reductions in falls [119-121]. While electronic systems for identifying drug-drug interactions have been in use for some time, CDSS is not yet in regular usage to

make recommendations on appropriateness of therapy since there is little firm evidence as of yet that CDSS can improve outcomes such as ADE occurrence rates.

Despite this, there is little doubt that CDSS and similar products will play an important role in prescribing optimisation in the future. Since doctors are caring for increasing numbers of patients over the age of 65, "*it is unrealistic to expect the majority of clinicians who prescribe for older people on a regular basis to possess the knowledge and experience and thereby have it inform their judgement when prescribing"* [52]. However, if tools like STOPP/START were available as commercial electronic software, evidence based electronic prescribing could be enhanced and provided quickly to the benefit of patients and doctors alike.

Advances are being made with regards to electronic application of STOPP/START. In 2012, a European research consortium received European Commission Seventh Framework Programme (FP7) funding to conduct a randomised controlled trial to develop, and test the efficacy of, a highly-powered and efficient software engine capable of individually screening the clinical status and pharmacological and non-pharmacological therapy of older people with multi-morbidity. The purpose of which is to define optimal drug therapy, highlight ADR risk, indicate best value drug brand for selection and provide advice on appropriate non-pharmacological therapy. The project entitled 'Development and clinical trials of a new Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons (**SENATOR**)' is being led by a University College Cork (UCC) research team, and includes five other sites around Europe, including the Scotland, Spain, Iceland, Italy and Belgium (www.senator-project.eu). The STOPP/START criteria have been

incorporated into the software engine and will therefore form the basis of recommendations on optimal drug therapy. The software will also advise clinicians on drug-drug and drug-disease interactions as well as non-pharmacological therapies which may benefit the patient e.g occupational therapy, physiotherapy or dietician intervention**.** The primary objective of the SENATOR project is to reduce incidence rates of ADRs in older patients, hospitalised with acute illness and will run until 2017. As mentioned earlier, research into CDSS has yet to show this as an achievable outcome.

Another project entitled 'Optimising Therapy to prevent avoidable hospital admissions in the Multi-morbid elderly (**OPERAM**)' has also recently received funding from the European Commission and Horizon 2020 scheme, and involves the same research team in UCC leading the SENATOR project. As with SENATOR, OPERAM will focus on addressing the pharmacotherapy optimisation needs of older patients with multi-morbid illnesses. The primary aim of OPERAM is to reduce re-hospitalization, composite health care and prescription costs in older patients in European. At the centre of the OPERAM project will be an RCT which aims to test the clinical and economic effectiveness of a new medication optimisation software package in elderly hospitalised patients in four academic teaching hospitals (University Hospital Berne, Cork University Hospital, Utrecht University Medical Centre and Saint Luc University Hospital Brussels).

OPERAM is closely linked to the outcomes of the SENATOR project. The OPERAM clinical trial will also involve a prescribing software intervention for older people with multi-morbidity which will be based on the second version of the

STOPP/START criteria. Given the potential of CDSS in general, and STOPP/START criteria in particular, it is likely that CDSS will complete clinical trials and pre-market validation in the coming years. The various intervention strategies that have been employed to date to address PIP are summarised in Table 1.

Table 1.1: Summary of intervention studies to date addressing PIP

Intervention Type	Study title	Authors/Year/Country	Summary of findings from all studies	Advantages	Disadvantages
Detection criteria	STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria The accuracy of medication histories in the hospital medical records of elderly persons	Gallagher *et al.*/2008/Ireland [36] Gallagher *et al.*/2011/Ireland [16] Beers et al./1999/USA [122]	STOPP/START guidelines most comprehensive in terms of research and applicability to other countries. Have shown good improvements in prescribing appropriateness. Has shown reduction in PIMs in 71% of patients	Concise. Most are consensus validated. Many highlight drug-drug interactions. Most address commonly prescribed drugs.	Most lack transferability and studies outside country of origin. Under-prescribing not addresses in most. Large amounts of clinical data required to apply some criteria. Time consuming
CGA	An outreach geriatric medication advisory service in residential aged care: a randomised controlled trial of case conferencing Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly Multifactorial intervention to prevent recurrent cardiovascular events in patients 75 years or older: the Drugs and Evidence-Based Medicine in the Elderly (DEBATE) study: a randomized controlled trial	Crotty *et al.*/2004/Australia[89] Schmader *et al.*/2004/USA[90] Strandberg *et al.*/2006/Finland [92]	55% improvement in MAI scores. Decreased risk of ADEs and decreased use of unnecessary drugs.	Patients' therapy is approached from a multidisciplinary view. Patients' cognitive and functional capacities are taken into account.	Time consuming. Resource intensive. Limited to hospital settings.

Table 1.1 Contd

Intervention Type	Study title	Authors/year/country	Main findings from available studies	Advantages	Disadvantages
Pharmacist review	Prevention of adverse drug reactions in hospitalised older patients using a software-supported structured pharmacist intervention: a randomised controlled trial. Does the addition of a pharmacist transition coordinator improve evidence based medication management and health outcomes in older adults moving from hospital to a long-term care facility? Results of a randomized controlled trial Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized controlled trial	O'Sullivan *et al.*/2013/Ireland [102] Crotty et al./2004/Australia [101] Spinewine et al./2007/Belgium [96]	24% improvement in MAI scores. Improvement in MAI scores was maintained at 12 months. No significant difference in ADEs except for most recent study which showed 7% reduction in ADR rates	Pharmacist is ideally placed to optimised older patients prescriptions. Can easily liaise with physicians and make recommendations regarding patients' prescriptions.	Not all pharmacists trained in geriatric pharmacotherapy. Resource intensive. No research showing improvement in ADE incidence rates.
Prescriber education	Effect of an educational intervention on optimizing antibiotic prescribing in long-term care facilities Inappropriate medication use in the elderly: results from a quality improvement project in 99 primary care practices Assessing the effects of an intervention by a pharmacist on prescribing and administration of hypnotics in nursing homes	Monette *et al.*/2007/Canada [115] Wessell *et al.*/2008/USA [116] Eide *et al.*/2001/Norway [117]	Reduced usage of PIMs. Improvements in overall prescribing appropriateness [109-112].	Direct interaction with the prescribers. Can be cost-effective and utilise less resources.	Much variation between types of educational interventions. Most studies tend to focus on particular drug classes rather than prescribing in general.

Table 1.1 Contd

Intervention Type	Study title	Authors/year/country	Main findings from available studies	Advantages	Disadvantages
CDSS	Prevention of adverse drug reactions in hospitalised older patients using a software-supported structured pharmacist intervention: a randomised controlled trial. Computerized clinical decision support during medication ordering for long-term care residents with renal insufficiency Effect of computerized provider order entry with clinical decision support on adverse drug events in the long-term care setting	O'Sullivan *et al.*/2013/Ireland [102] Field *et al.*/2009/USA [123] Gurwitz *et al.*/2008/USA [121]	Reduction in initiation of PIMs. Overall improvement in prescribing appropriateness. Significant reduction in ADEs in most recent study [102]	Clinicians automatically provided with evidenced based recommendations helping them to make more informed decisions. Clinicians with less knowledge/experience can feel more confident about their prescribing decisions.	In general, CDSS do not advise on appropriateness of prescribing. Depend on quality of computer programming. Costly and difficult to implement on a large scale**.**

Key: RCT=Randomised controlled trial **CGA**=Comprehensive geriatric assessment **CDSS**=Computerised decision support systems **MAI**=Medication appropriateness index **ADE**=Adverse drug event **ADR**=Adverse Drug Reaction **PIM**=Potentially inappropriate medication

1.5 Evolution of interventions in healthcare

Healthcare intervention trials occupy much of the medical literature today. These range from simple 'before and after' studies quantifying the effect of a new policy, process or drug [124], to more complex RCTs comprising multiple components which may act both independently and interdependently of each other [125]. The method of delivery has understandably seen a shift in recent years from face to face interactions to interventions delivered via the internet [126-137]. Reasons proposed by authors for choosing internet based interventions include: reducing cost and increasing convenience for users; reducing health service costs; reducing isolation of users; the need for timely information; reduction of stigma; increased user and supplier control of the intervention [124].

One of the most significant ongoing changes in intervention research is the process by which intervention studies are informed. Historically, many intervention studies have not described in detail why the intervention type was chosen. In more recent times however there has been much research published regarding intervention mapping [138-142], i.e. tailoring the intervention to specifically target the barriers associated with the behaviour in question. The identification of these barriers is the key step in this process, and one which has only recently begun to receive attention.

Barriers to best practice can be identified through qualitative research. Qualitative methodologies are being used more and more to uncover the causative factors of various healthcare problems and to gain insights into healthcare professionals'

attitudes and other factors which affect their decision making [143-150]. In this way, the processes that lead to sub-optimal practice are uncovered, and can then form the basis of an intervention. **Figure 1.2** illustrates how qualitative research studies have become more prevalent in recent years.

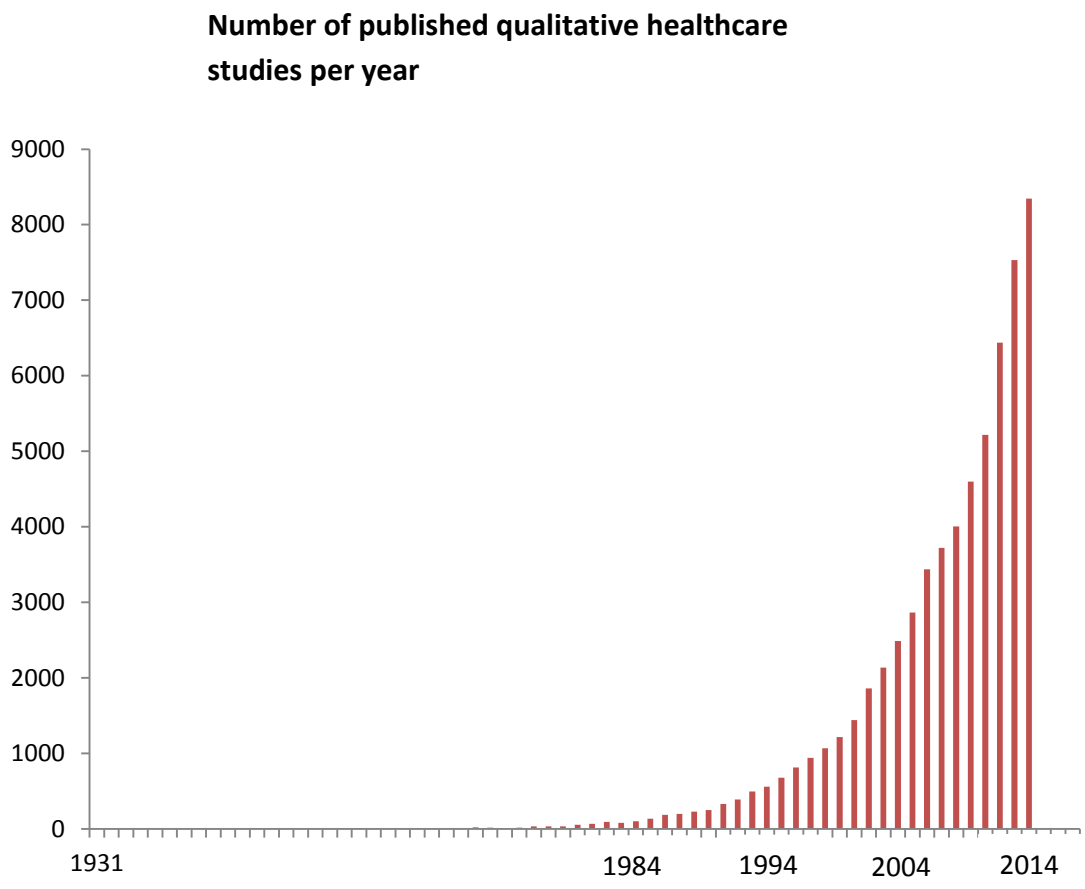


Figure 1.2 Increasing trend of qualitative healthcare studies in recent years (Pubmed)

Figure 1.2 shows that before the mid 1980's, very little qualitative research was taking place in healthcare. However since then, with increasing literature highlighting the potential of qualitative methodologies [151, 152], there has been an exponential increase in the number of studies employing such methods.

Qualitative research was first used by sociologists and anthropologists in the early twentieth century. It remained a research tool of the social sciences for many years until the 1960s, when the development of grounded theory and ethnography saw qualitative methods being implemented in other areas of research qualitative research. Researchers, including healthcare professionals, have in recent decades seen to see the benefits of this type of research and are modifying these approaches to the study needs of their own areas.

Qualitative research is sometimes thought of as the alternative to quantitative methods as it does not aim to quantify outcomes with statistics and figures. Qualitative research is inductive in nature and relies on interviews, surveys, focus groups and observation for data collection [151]. In healthcare research, the interview is the most commonly utilised tool. There are three types of interviews: structured, semi-structured and unstructured. The semi-structured interview is more commonly used in health care-related qualitative research [151]. It is typically based on a topic guide that provides a flexible and loose structure of open-ended questions to explore experiences and attitudes. The topic guide is, as the name suggests, just a guide, and the interview is steered more by the interviewees' responses and descriptions of their own experiences and attitudes.

Both quantitative and qualitative research have particular strengths and limitations, but recently, researchers have recognised that it is not a case of choosing one over the other, but rather using the two to complement each other [153]. Murphy *et al.* comment that "*true understanding in medicine cannot be achieved without adding*

qualitative methods to the research arsenal" [154]. For instance RCTs are the standard means of testing the effect of an intervention or a treatment. However, should one wish to determine why results from research or well established best practices are not being implemented, qualitative methods are more suited to elicit participants beliefs and own experiences with regards to the practice in question [151]. Similarly, before designing an intervention based on quantitative methods, a qualitative study identifying participants beliefs and opinions as to the barriers that exist to best practice being implemented can inform that intervention and ultimately enhance efficacy [139]. The type of question being asked should guide the methodologies used [155]. Put simply, quantitative research addresses questions such as 'how much and how often? Qualitative research explores the reasons *why*. To really investigate and address a problem, both types of questions need to be asked.

Although qualitative research is used increasingly in healthcare, there is very little qualitative research into PIP in older people [156]. Most of the studies in the literature only focus on a particular drug class rather than prescribing in general [156]. As stated earlier in this chapter, to date, few of the intervention studies aiming to reduce PIP in older patients have been informed by previous qualitative studies. It cannot be said with certainty that this is a contributory factor to the mild/moderate level of success of such interventions. However, with qualitative research in general, and interventions *informed* by qualitative research in particular, proving to be successful in other areas of healthcare, including

prescribing [157-162], it is reasonable to propose that future intervention designs targeting PIP, should have an element of qualitative inquiry.

1.6 Summary

PIP in older patients is a major global healthcare problem today. The global population is ageing and with this comes a greater burden of diseases, increased numbers of medications and increased strain on health systems and resources. All these factors make for favourable circumstances for PIP to occur, indicating that the problem is only going to worsen in the years to come in tandem with global ageing. Some strategies implemented to date to counteract PIP have shown promise but many have also shown lack of applicability to everyday practice. To enhance the efficacy of future interventions, qualitative research is needed to identify the barriers to appropriate prescribing. In this way, interventions can be tailored to address the specific causative factors of PIP and ultimately improve prescribing appropriateness for older patients.

2. A meta-synthesis of potentially inappropriate prescribing in older patients

Chapter description

The quantitative aspect of this thesis was to be informed by qualitative research. Therefore, a systematic review of the qualitative research already published was deemed appropriate.

The work of this chapter has been published as Cullinan S, O'Mahony D, Fleming A, Byrne S. A Meta-Synthesis of Potentially Inappropriate Prescribing in Older Patients. Drugs & Aging. 2014;31(8):631-8. http://dx.doi.org/10.1007/s40266-014-0190-4 (Appendix I)

2.1 Introduction

Potentially inappropriate prescribing (PIP) is commonly seen amongst the older population. There are various factors that make this group more susceptible to PIP, principally multiple co-morbidities and related polypharmacy [13, 163]. PIP includes both prescribing of potentially inappropriate medications (PIMs) i.e. introducing a medication that poses more risk than benefit when a safer alternative is available, as well as potential prescribing omissions (PPOs) [11, 13, 17, 52, 164] i.e the omission of medications that would likely benefit the patient. In primary care, recent studies show that 20-40% of older patients have PIP [13, 163, 164]. The prevalence of PIP in older people ranges from 33% to 58% in the hospital setting [11, 52] and from 44% to 70% in long term care facilities [17]. The common consequences of PIP are adverse drug reactions (ADRs), adverse drug events (ADEs), increased hospitalisation and inefficient use of resources [41, 165, 166]. Consequently, PIP places a large economic strain on the health care system and intangible costs on individuals.

Quantitative data such as these have highlighted the issue of PIP and attracted attention to its economic implications. However, very little attention has been focused on *why* it is occurring. This chapter aims to synthesise qualitative studies that explore PIP in older patients in an effort to understand the psychological and behavioural basis of PIP applied to older people and to generate a new theory to guide future intervention studies aimed at PIP prevention. The small number of qualitative studies in the published literature has never previously been analysed in a meta-synthesis such as this before. Application of qualitative research methods in

a variety of health care research domains [167] has provided important insights and understanding with relevance to clinical practice.

As with meta-analysis of data from quantitative studies, meta-synthesis of qualitative studies involves a recognised methodology for combining the themes from several studies. However, unlike a meta-analysis, a qualitative synthesis aims to interpret the thematic findings from the original studies so as to be able to generate new, all-encompassing theory not previously identified [167-170]. To do this, a technique called meta-ethnography [171] was employed, which has been used to good effect in health care research [167, 170, 172, 173].

2.2 Methods

The seven step model of meta-ethnography (**Figure 2.1**) was used, i.e.
In step 1, a clear statement of the specific research question was agreed.

In step 2, a *search strategy* to identify suitable articles was developed. Four databases were systematically searched for papers published up to the end of April 2013 (no start date was specified): PubMed, Embase, CINAHL and Web of Knowledge. The following terms were used: Qualitative AND (Inappropriate* OR Appropriat* OR Safe) AND (Elderly OR Aged OR Geriatric* OR Old*) AND Prescri*. The reference lists of papers identified were then searched for other suitable papers that should be included in the meta-synthesis.

Papers were deemed suitable for inclusion if they used qualitative methods, explored some area of PIP in patients over 65 years of age, were published in English and had available published abstracts. Two co-researchers then read articles

that were deemed potentially relevant after the abstract review. Articles meeting inclusion criteria were included in the final review.

The quality of the final papers was assessed by two researchers using the Critical Appraisal Skills Programme (CASP) (Appendix II). The CASP tool assesses qualitative papers on the basis of the results presented, the validity of the results and the potential implications of the results locally. The CASP methodology was employed as it has been used to good effect previously in healthcare research studies [167, 169, 172, 174]. The purpose of using CASP was not to eliminate published papers, but rather to make sure the papers that were used were of high quality, and to ensure low quality papers were not contributing to our final synthesis.

Step 3 involved *reading the studies.* The terms first order, second order and third order constructs relate to the different levels of interpretation within a meta-synthesis. First order constructs relate to the raw data in the empirical studies i.e the original participants' interpretations of a certain experience. Second order constructs are the common themes/categories that the original authors identified amongst these participants and used as their results/findings. Third order constructs are the *new* interpretations that those performing the synthesis must identify by compiling all the second order constructs from the selected studies, translating them into each other to determine if in fact they concur in terms of thematic content, and then reinterpreting them to generate new theory. The papers were read carefully by two researchers, including the present author. The key findings from each paper, as presented by the authors, were listed as the second order constructs.

In step 4 , it was determined how the studies were related to each other by listing key concepts that represented the whole data set.

In step 5, the papers were translated into each other. There are numerous forms of final synthesis within meta-ethnography, the choice of which depends on how the papers are related to each other [171]. As it became apparent that concepts from one study would encompass others, if not all the other studies, 'reciprocal translation' was used followed by 'line of argument' synthesis. Each key concept was compared across the published papers, to determine what each paper stated about that concept. In this way, the papers were translated into one another.

Step 6 involved examining what each paper stated about each concept, and reinterpreting these to produce third order constructs, linked together in a final 'line of argument synthesis'. The aim of a 'line of argument' is to create a coherent theme that may explain what all the studies have reported in one holistic theme, taking into account the fact that each study may have explored different aspects of the phenomenon [175].

Finally, in step 7, the results of the synthesis were expressed in tables, figures and text. The ENTREQ (Enhancing transparency in reporting the synthesis of qualitative research) [176] statement, a framework for reporting the synthesis of qualitative health research, was used to guide how the results were reported.

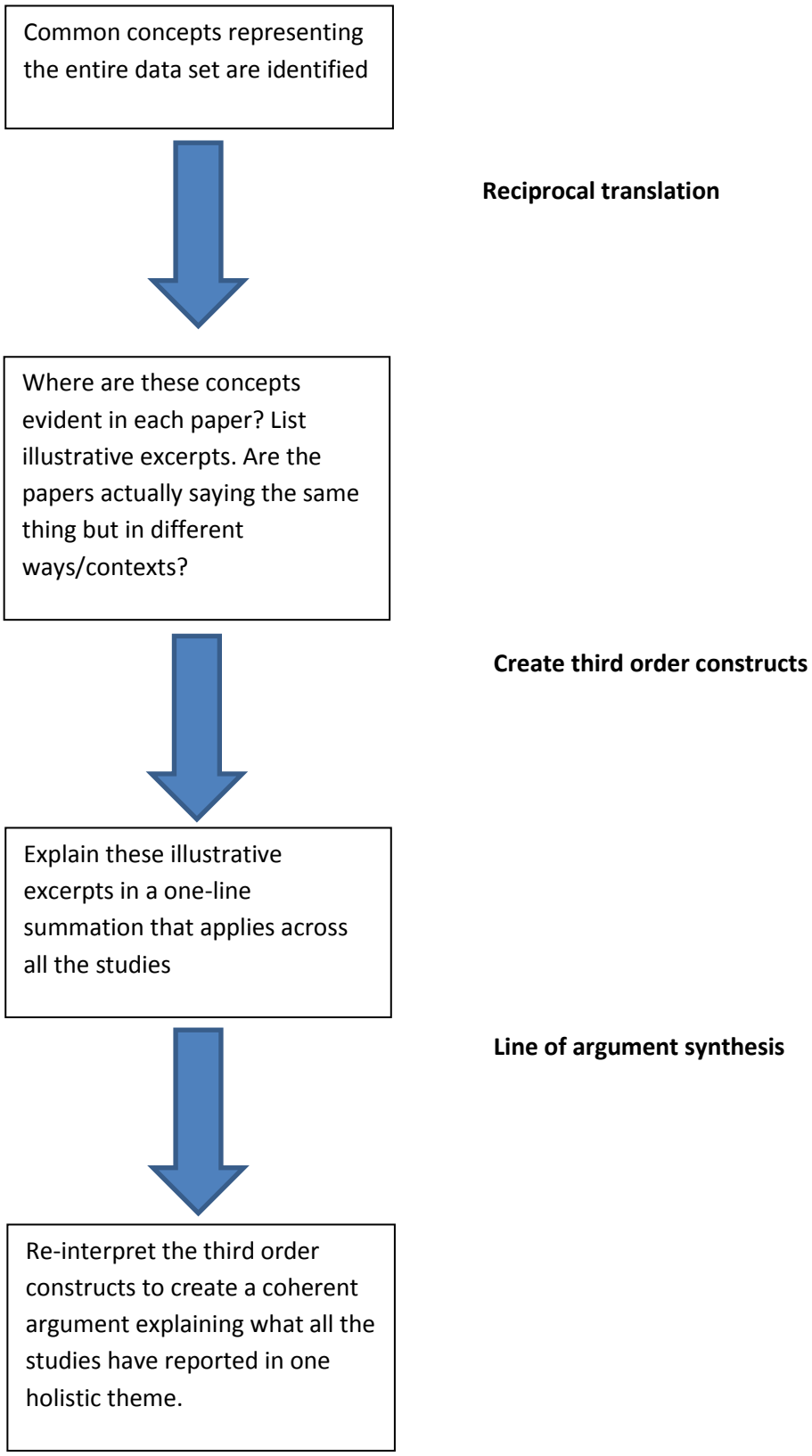


Figure 2.1: Flow diagram of meta-ethnography process

2.3 Results

The PRISMA checklist was followed with regards to the writing of this study (see appendix III).

The search of the electronic databases identified 864 papers, leaving 624 after duplicates were removed (**Figure 2.2**). After title and abstract review, a further 576 studies were removed: 348 did not use qualitative methods, 176 did not involve PIP, 44 did not deal with patients over 65 and 8 had no abstracts available. Sixteen full papers were retrieved for review. Of these, 10 were eliminated because they did not use qualitative methods. One additional paper was identified from the references list of another paper and included. This left seven papers for inclusion in final synthesis (**Table 2.1**).

All seven papers were of high quality according to the CASP criteria; all of the papers met most of the criteria for inclusion in the analysis. Common weaknesses were 'reflexivity' (the awareness of the *researcher's* contribution to the construction of meanings throughout the research process), which none of the papers mentioned, 'data collection' (none of the papers justified methods chosen or discussed saturation of data) and 'statement of findings' (the majority of papers did not apply triangulation i.e the use of multiple data sources).

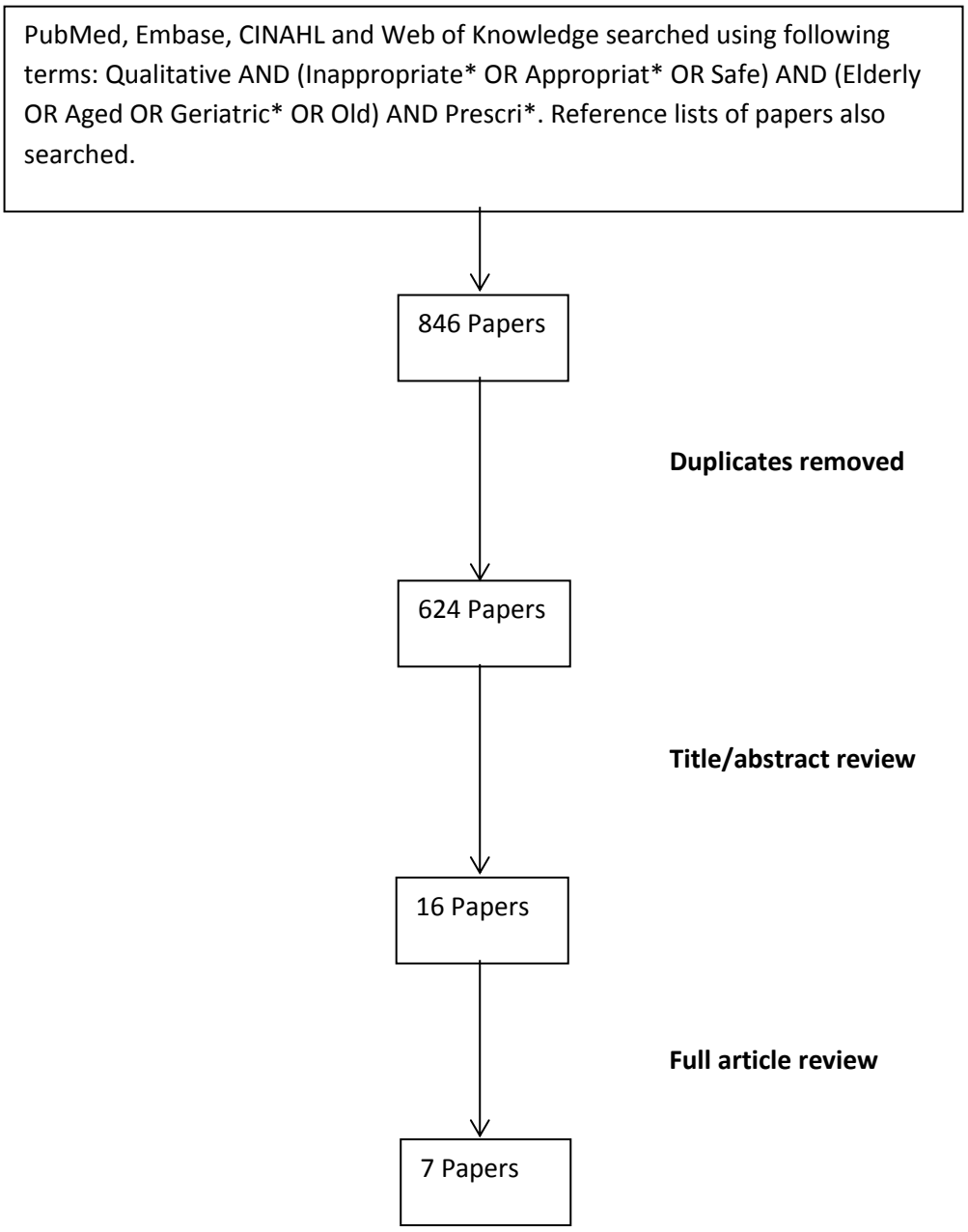


Figure 2.2: PRISMA flow diagram of literature review process

Table 2.1: Characteristics of papers identified

	Paper title (year of publication)	Authors	Country	Sample size (n)	Methodology	Method(s)
1	Prescribing psychotropic medication for elderly patients: some physicians perspectives (1999)	Damestoy *et al*[157]	Canada	9 doctors	Grounded theory.	Semi-structured interviews
2	Appropriateness of use of medicines in elderly inpatients: qualitative study (2005)	Spinewine *et al*[177]	Belgium	5 doctors 4 nurses 3 pharmacists 17 patients	Grounded theory.	Semi-structured interviews, focus groups and observation
3	Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study (2007)	Cook *et al*[158]	USA	33 GPs	Narrative analysis.	Semi-structured interviews.
4	GPs' approach to insulin prescribing in older patients: a qualitative study (2008)	Agarwal *et al*[159]	Canada	21 GPs	Grounded theory.	Semi-structured interviews.
5	Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study (2008)	Wood-Mitchell *et al*[160]	England	8 consultant Psychiatrists	Grounded theory.	Semi-structured interviews.
6	Long-term prescribing of antidepressants in the older population: a qualitative study (2010)	Dickinson *et al*[161]	England	36 patients 10 GPs	Framework analysis.	Semi-structured interviews.
7	Primary care providers' perspective on prescribing opioids to older adults with chronic non-cancer pain: a qualitative study (2011)	Spitz *et al*[162]	USA	23 doctors 3 nurse practitioners	Thematic analysis.	Focus groups

GP=General practitioner

2.3.1 Reciprocal translation

Four key concepts that reflected the findings in the 7 papers were identified from the meta-synthesis as being contributory factors to PIP:

(i) Desire to please the patient

(ii) Feeling of being forced to prescribe

(iii) Tension between experience and guidelines

(iv) Prescriber fear.

The reciprocal translation and final synthesis are presented below. Each of these thematic concepts is described in greater detail. Excerpts consisting of original quotes from participants (first order constructs) as well as authors' findings (second order constructs), from the original papers are presented in **Table 2.2** along with third order interpretations to illustrate how the four themes were identified.

2.3.1.1 Desire to please the patient

In the majority of papers, there was a clear underlying theme of 'wanting to please the patient'. This usually meant prescribing outside the guidelines. As Dickinson *et al.* stated in their paper exploring inappropriate long-term prescribing of antidepressants, '*..in many circumstances it is easier to follow the path of least resistance and let them (i.e. PIP decisions) be..*'[161]. This was a common viewpoint expressed by the doctors they interviewed. They noted that patients were happy with their antidepressants and as a result doctors were generally satisfied with the pharmacotherapy. They also observed that the doctors recognised the problem of prescribing medication even though the problem may be social rather than

psychiatric in nature. However, due to some patients' resistance to non-pharmacological treatments, they proceeded with prescribing the medication anyway.

Agarwal *et al*. refers to this resistance from patients' in their study of GPs' approach to insulin prescribing in older patients [159]. When asked why insulin is often under-prescribed in this population, the consensus was that '*GPs felt older patients would be less receptive to medication regimen changes*'. Spitz *et al* examined underuse of opioids in older patients for non-cancer pain [162]. In this study, the patient was also a common barrier to appropriate prescribing, apparently as a result of older patients' reluctance to consider opioid analgesia for this category of pain. The physician participants in this study also commented that this resistance acted as a barrier to prescribing these medications to future patients.

The concept of prescribing to please the patient was most evident in the paper by Cook *et al* [158] who explored prescribers' attitudes to prescribing benzodiazepines for older adults. It is generally accepted that these medications should only be used for brief periods in older patients and for symptomatic relief only [178, 179]. The participants in this study spoke of the problems they experienced in the past with trying to wean patients off benzodiazepines and how this affected their future prescribing patterns. The participants again spoke of '*the path of least resistance*' and how much quicker and easier it is just to prescribe what the patient wants, rather than spend significant amounts of time trying to persuade patients towards a different approach to managing insomnia and anxiety. They furthermore identified the possibility of the patients switching to another physician as a reason

for inappropriate prescribing. This was also reported by Damestoy *et al*, who studied physicians' perspectives on prescribing psychotropic medication for older patients [157]. The participants described how otherwise quiet and timid patients became aggressive and demanding when their anxiolytic use was questioned.

*2.3.1.2 **Forced to prescribe***

One consequence of this need to please the patient was that prescribers often felt they were forced into prescribing, or not prescribing medications, in a manner they knew did not adhere to guidelines. This concept could therefore have been integrated into the previous one, however upon consideration it was decided it should stand alone, as there were several factors leading prescribers to feeling forced to prescribe, other than the need to please the patient e.g. poor quality of treatment resources. Wood-Mitchell *et al* explored prescribing of medications for dementia in older patients [160]. They observed that many of the prescribers felt they were seeing too many referred patients due to a lack of support services for these patients. According to many prescribers, there was too much reliance on medication as a quick and 'easy' treatment for these patients and the development of non-pharmacological treatments was deployed less frequently as a result. Also, the quality of care settings was important in the prescribers' decision process. Low quality training of care staff and 'under-stimulating environments' were thought to result in challenging behaviours in demented patients. These low quality care facilities are then unable to cope with disturbed patient behaviour and are more likely to refer the patients for assessment with a view to pharmacotherapy for their disturbed behaviour. The physician prescribers then feel they have no choice but to prescribe due the lack of services already mentioned.

Agarwal *et al* also reported this lack of confidence amongst prescribers in some long term care settings [159]. In relation to not prescribing insulin, GPs' knowledge of some care facilities hindered them from starting a patient on insulin due to the doctor's lack of confidence in the support the patient would receive in care. Lack of therapeutic alternatives was another factor leading to physicians feeling forced to offer pharmacotherapy. Damestoy *et al* described how doctors felt that non-pharmacological treatments were insufficient for conditions such as anxiety [157], indicating that many doctors *'considered them to be ineffective* (and that)….*psychotherapeutic approaches were doomed to failure*'. This was echoed by Wood-Mitchell *et al* [160]. And again by Dickinson *et al*, indicating long waiting lists for cognitive behavioural therapy [161]. Damestoy *et al* [157] also identified a feeling of isolation amongst prescribers, once again forcing them to prescribe in some situations where they realize that psychotropic medications are not appropriate. This theme of 'isolation' was also picked up by Spitz *et al* [162] reporting that doctors desired more peer support to enable them to prescribe appropriately. Looking at these studies, it can be seen that prescribers usually know what appropriate treatment is, but feel unable to follow through.

*2.3.1.3 **Experience VS Guidelines***

In all but one of the papers, it was clear that prescribers were well aware of the potentially inappropriate nature of some of their prescribing. They were, for the most part, aware of the treatment guidelines and they all agreed as to what the best practise was. However, in general, they varied greatly in their actual prescribing practise. Although they accepted the precepts of the guidelines, they perceived a significant problem in implementing them in real life. The end result

was reversion to previous practises, and what they were familiar with. Lack of evidence supporting some guidelines also influenced prescribers in favour of his/her own experiential evidence as reported by Woods-Mitchell *et al* [160]. Conversely, Agarwal *et al* [159] reported that a prescribers' *lack* of experience can have a similar effect in relation to under-prescribing of insulin.

Cook *et al* [158] found that many prescribers considered that guidelines were '*out of touch with real world problems'* and that past experience had taught them to avoid changing drug therapy in order to avoid a perceived higher risk of misadventure. Damestoy *et al* [157] reported that many of the physicians interviewed prescribed as they did because they didn't often see side-effects. Spitz *et al* [162] used focus groups with prescribers to elucidate why opioids were underused in non-cancer pain in older people. They found that doctors were aware that opioids have a role in non-cancer pain, but felt the evidence base was insufficient to support this role. They also expressed their desire for evidence-based tools for calculating doses. Dickinson *et al* [161] showed that in relation to long term prescribing of antidepressants, GPs didn't perceive a significant problem, as they hadn't seen any evidence to indicate serious harm to older patient.

2.3.1.4 ***Fear***

The final concept evident across the papers reviewed was fear. It manifested itself in a number of different ways but in each case it was clear that it was a contributing factor to PIP. For instance Agarwal *et al* [159] reported that doctors felt a sense of apprehension towards older patients in general due to their higher prevalence of frailty and co-morbidities. Consequently, they perceived more potential to do harm. They also observed a fear of the unknown amongst several GPs e.g. most admitted

to inexperience using insulin in older patients and found the prospect of initiating it anxiety-provoking, such that they would avoid prescribing it even if guidelines recommended it.

Dickinson *et al* [161] also identified fear as a central theme amongst GPs in relation to PIP. Doctors described reluctance to discontinue a medication that has been taken for a long time by a patient in order to avoid worry, and spoke of not wishing to disrupt patients' clinical stability. With this observation of fear of medication change and an apparent lack of fear of side effects, (also reported), these authors concluded that there was just no incentive for medication change. Fear of causing harm was the overwhelming barrier identified in the study by Spitz *et al* [162]. For example, prescribers described genuine fear of prescribing opioids for older patients, and worry regarding the possible serious side effects. Sometimes these fears arose from previous bad experiences with prescribing opioids in older patients. In other cases, this fear was more to do with avoidance of the guilt that would ensue if a patient was to have an adverse drug event due to the drug. Spinewine *et al*, observed a different kind of fear in their study looking at appropriateness of medicines in general in older patients [180]. Prescribers they interviewed described a fear of offending other doctors, including specialist doctors and GPs. If, for example, a doctor noticed something potentially inappropriate on a patient's prescription, but if that patient was under the care of a specialist, they would be less likely to intervene. Similarly, when transferring information between levels of care, e.g. from hospital to primary care , it was noted that the amount of information could be limited due to fear of causing offence to patients' GPs.

Table 2.2: Excerpts supporting the four themes plus third order interpretations

	Excerpts (first and second order constructs)	Paper(s)	Third order interpretations
Desire to please the patient	They [antidepressants] allow the doctor and the patient a feeling of doing something in the face of unsolvable problems.	Dickinson *et al* *[161]*	The patient can have too much of a deciding role in their therapy at times. This sometimes hinders the doctor from making their decision based purely on what is the best course of action for this patient.
	There appeared to be some sense of unease about prescribing a medical intervention for a social cause……the goal of both doctor and patient appears to be not to rock the boat.	Dickinson *et al* *[161]*	
	Prospects ranged from questioning the doctor's authority and competence, to minimisation of negative side-effects, to finding another doctor who was willing to prescribe it.	Cook *et al* *[158]*	
	Many of the physicians thought patients would seek out another physician if they were not satisfied with their prescription, and they took this into account before prescribing.	Damestoy *et al* *[157]*	
Feeling forced to prescribe	Some participants felt that certain homes coped better than others with problematic behaviours and one thought it depended on whether beds needed to be filled.	Wood-Mitchell *et al* *[160]*	Due to a combination of intrinsic and extrinsic factors, and although they may realise it is not quite appropriate, doctors are sometimes left with no other choice but to prescribe, or not prescribe, in an inappropriate fashion.
	GPs also described situations where their own experiences or knowledge of particular nursing homes or less-than-ideal care situations, hindered them from considering insulin treatment	Agarwal *et al* *[159]*	
	All participants felt strongly that there was a pressure to prescribe and that the availability of alternatives to medication influenced decisions.	Wood-Mitchell *et al* *[160]*	
	One frequently cited reason for the favouring of antidepressants was the inadequacy or unavailability of alternative treatments.	Dickinson *et al* *[161]*	
	They recognised that the inappropriate use of psychotropic medication for elderly patients was a public health problem, but they felt it was beyond the scope of the individual physician.	Damestoy *et al* *[157]*	

Table 2.2 (continued)

Experience Vs Guidelines	In most cases, choice of medication was based on familiarity and past experience of a drug…..the influence of evidence base had a varying effect on the participants. Most GPs had little experience of treating older patients with insulin. This lack of experience made some apprehensive about initiating it. In the absence of evidence of specific adverse effects, there was little concern.	Woods-Mitchell *et al* [160] Agarwal *et al* [159] Dickinson *et al* [161]	Past experience, or lack thereof, can sometimes over-ride guidelines or the appropriate decisions. Sometimes this may simply be necessary and actually be appropriate, however, the literature suggests it is also contributing to PIP.
Prescriber fear	Two doctors acknowledged that information transferred to general practitioners could be limited by fear of offending them with comments on inappropriate prescribing. *'It's scary to stop a medication that's been going on a long time, because you think am I opening a can of worms here'* *'I get frightened with 80+ year olds; how are they going to respond?'*	Spinewine et al[177] Dickinson *et al* [161] Spitz *et al* [162]	Fear is a multifactorial component of PIP. While not likely to be the major cause of inappropriate prescribing, it would seem to compound already existing factors, thereby contributing to the overall effect.

GP=General practitioner

2.3.2 Line of argument synthesis

Looking at the four key concepts that emerged from the papers, it was concluded from the literature that, in many situations, prescribers suffer from 'self-perceived restrictions' leading to a sense of powerlessness to prescribe appropriately for older patients. This powerlessness in turn forces them to rely on what they know and have done before (previous habits/experience), which leads to the PIP that has been identified [11, 17, 41, 52, 165]. **Figure 2.3** illustrates the line of argument synthesis.

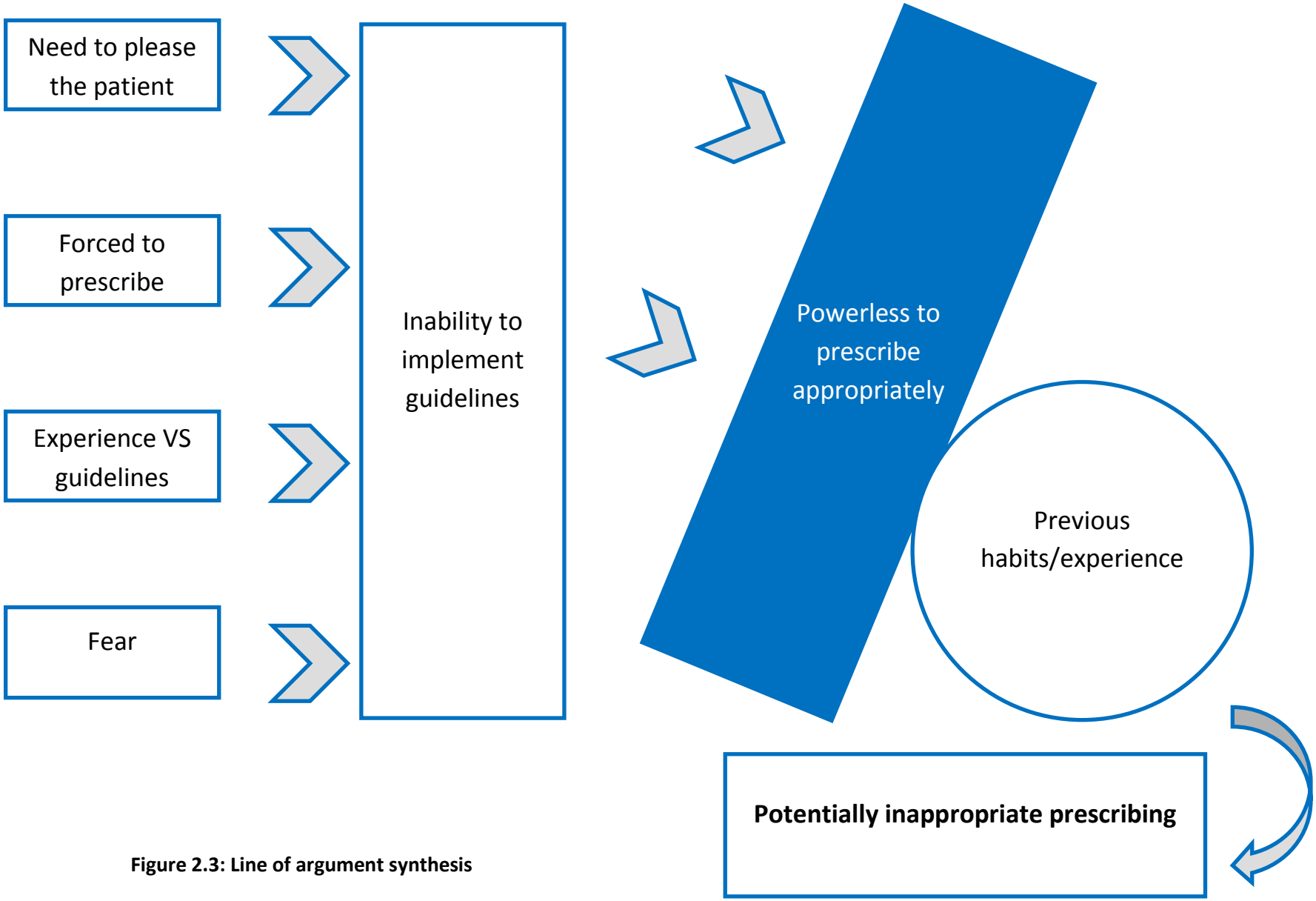


Figure 2.3: Line of argument synthesis

2.4 Discussion

Although the published literature abounds with papers describing the prevalence of PIP in various clinical settings and the link between PIP and multi-morbidity/polypharmacy in older people, there is a lack of detailed inquiry into the prescriber-based reasons that underpin PIP. This meta-synthesis has, for the first time, identified a cluster of reasons why physicians feel may perpetuate PIP in older people. The principal reasons include:

(i) The need to please the patient

(ii) Feeling forced to prescribe

(iii) Tension between prescribing experience and prescribing guidelines

(iv) Prescriber fear.

Ultimately, these factors in combination militate against safe and effective prescribing in older people.

At the outset, this chapter aimed to achieve an understanding of why inappropriate prescribing occurs in older patients. This analysis, of course, involves *all* medication classes. It was unclear therefore, whether the selected papers would be suitable as six out of the seven focused on individual drug classes. Each paper was based on evidence that a certain amount of PIP was occurring within a certain class of drug. However, upon reading the papers and through reciprocal translation it became clear that although each study explored different areas of prescribing, and in significantly different settings, for the most part, similar themes were present amongst them all. This is encouraging since it suggests that measures taken to

address the issues highlighted here, will likely lead to improvements in all areas of prescribing, not just in one specific drug class.

The line of argument synthesis suggested that doctors know the guidelines and for the most part, have no opposition them. They know that some of their prescribing is inappropriate, but feel powerless to do anything about it due to the pressures exerted on them in the key areas identified. This would suggest that future attempts to improve prescribing should not be focused on guidelines but rather on the issues that prevent these guidelines being implemented. Some of these issues can certainly be addressed and rectified, but others are more challenging. For example, patient education would very likely go a long way to helping prescribers when it comes to difficult decisions regarding patients' prescriptions such as stopping, or reducing the dose of a drug.

Looking at the concept of 'please the patient' identified from these studies, it is clear that resistance to change from the patient, previous bad experiences with patients and fear of losing patients to other doctors are significant contributing factors to a prescriber's decision making process, and that can ultimately lead to inappropriate prescribing. It is interesting that prescribers are aware of this. Studies have shown that patient-centred educational programmes are effective, and significantly reduce inappropriate prescribing [181, 182]. If patients were better informed, prescribers may encounter less resistance to change, and be less worried about losing patients to other practises.

One major factor contributing to prescribers' feelings of being forced into decisions was the lack of resources available. On a large scale, this is difficult to rectify due

mainly to financial constraints. However, better use of the resources already available would be a start. For example, simple improvements in communication between different levels of care may address the feeling of isolation that doctors reported. It would also improve their confidence to prescribe outside their usual remits if the prescribing process has a greater multidisciplinary approach. This would also address the 'fear of offending other physicians' observed amongst prescribers. The concept of information sharing and feedback has already been shown to reduce inappropriate prescribing with respect to input from pharmacists, especially in secondary care [183, 184]. The other issues raised within the 'fear' domain were fear of doing harm and fear of the limitations of prescribers' own capabilities. Prescriber education, although it certainly exists, probably needs to focus more on older patients. Greater input from geriatricians would be invaluable to GPs and others who regularly prescribe for this population.

It is important to note that much of what prescribers expressed in these studies in terms of reasons for prescribing in the manner they do, is valid and may be perfectly appropriate in many cases. For example, few would argue with a doctor being more concerned with the quality of life of a patient rather than strict adherence to the guidelines. Equally, there are few objections to doctors prescribing drugs 'off label' if they are convinced that such prescriptions are of benefit to particular patients. However, as stated, PIP has been shown to be a significant problem leading to increased costs and adverse drug events. Some of the prescribing which would technically be labelled as 'inappropriate' may in reality be considered quite acceptable by some prescribe. However, there is still a proportion

of prescriptions that are clearly inappropriate, and of which, prescribers are aware. It is clear from reviewing these studies that past experience of a drug or treatment regimen can have more influence on prescribers' decisions than evidence base and guidelines. This reliance on 'what they have done before' feeds into a repetitive cycle that is more likely to result in PIP.

To date, there is a lack of proven interventions that reliably counteract PIP in older patients. A recent review by O'Connor *et al* [52] points towards 4 potential areas of intervention to counteract PIP in this population, namely comprehensive geriatric assessment, medication use review, prescriber education/audit/feedback and computerized prescriber order entry with clinical decision support. However, the evidence to support routine implementation of any of these interventions to prevent PIP in multi-morbid older patients so far is weak. Prescriber education interventions to prevent PIP in particular drug classes have been shown to work, e.g. antibiotics, opioid analgesics and antipsychotics [52]. However, interventions to steer prescribers away from PIP in older patients in the broad sense are lacking. Rather surprisingly, researchers have given relatively little attention to *prescriber decision-making* as a prime target for attenuating PIP in the high-risk older multi-morbid population.

There may be other prescriber factors to consider other than the 4 prime reasons that predispose physicians to poor prescribing practices identified in this study. Nevertheless, these findings provide an evidence-based platform for design of more effective interventions as a means of PIP prevention in elderly populations. Whatever interventions are developed in the future, they should empower

physicians to prescribe in such a way as to improve adherence to guidelines, avoid feelings of being forced to prescribe inappropriately in order to please patients, and minimise fear of countermanding other physicians' prescriptions.

The global expansion of the frail older population demands an improved level of education in geriatric pharmacology at undergraduate and postgraduate level. Specifically, this will involve electronic education programmes that include self-testing and feedback. Importantly, recent discourse on prescriber 'non-technical skills' has cast new light on a previously neglected aspect of prescriber behaviour [185]. These 'non-technical skills' encompass communication, team-working/leadership, error awareness, risk assessment and situational awareness. This skill set must be incorporated into any prescriber education programme to enhance its efficacy. A model for the delivery of such an intervention has been suggested [185].

2.5 Limitations

Although a systematic search was carried out for suitable papers, qualitative papers are often difficult to find due to ambiguous titles.

Meta-ethnography, while a useful tool for this kind of research, is not an objective technique and is open to differing interpretations between different researchers. Therefore, while credibility, transferability and dependability are provided for by utilising well-established methods, the confirmability of the findings cannot be assured.

Four of the seven papers included in this review concerned the prescribing of psychiatric medications. Mediators of PIP may differ between psychiatry and other areas of medicine. Similarly, the mediators of the different forms of PIP (PIMs and PPOs) may differ. PIMs and PPOs were not separated for individual analysis in this paper.

2.6 Conclusion

PIP in older patients is a result of many factors, including patient-level, prescriber-level and system-level barriers that result in prescribers feeling unable to prescribe in an appropriate manner. Possible remedies for this situation include better communication, more comprehensive education and system-level interventions to enable prescribers re-acquire this power. The problem is not a lack of prescribing guidelines, rather it is an abundance of barriers to implementing these guidelines, which need to be systematically removed.

3. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalised patients: A qualitative study

Chapter description

Given the lack of published qualitative research in the area of PIP in older patients highlighted in Chapter 2, it was decided to carry out an empirical qualitative study, both to add to the literature as well as guide and inform the next stages of research for this thesis.

The work of this chapter has been published as Cullinan S, Fleming A, O'Mahony D, Ryan C, O'Sullivan D, Gallagher P, et al. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalized patients: A qualitative study. British journal of clinical pharmacology. 2014. DOI: 10.1111/bcp.12555 (AppendixIV)

3.1 Introduction

As indicated in chapter 1, the population is ageing globally. Recent projections estimate that by 2018, there will be more people over the age of 65 years, than there will children under 5 years worldwide [186]. By 2040, 1.3 billion people will be over 65 years of age, an increase from the current 7% of the worlds' population to 14% [186]. As well as economic progress globally, advances in diagnostics, treatment, and in healthy-living initiatives, are largely responsible for this population growth [186]. The prescribing of multiple medications for multiple disease states, is common amongst older individuals, and these patients are therefore more vulnerable to medication related problems, including potentially inappropriate prescribing (PIP) [187, 188].

Whilst it is acknowledged in the literature that PIP is an issue requiring significant attention, little qualitative research has been conducted into *why* PIP occurs. This was highlighted in Chapter 2. Indeed, studies investigating PIP have traditionally focused on the individual medicines or pharmacological class of medicines that are inappropriately prescribed [157, 159, 160, 162, 189, 190]. However, one study conducted by Spinewine *et al.* investigated contributory factors to PIP in general, and reported that reliance on acute general care, a passive attitude towards learning and a paternalistic relationship between doctor and patient all contributed to PIP [180].

Behaviour change is key to any intervention requiring improvement in clinical practice. For example, Boscart *et al* demonstrated the benefits of applying psychological theory to inform a behaviour change intervention [191]. They

examined barriers and facilitators to hand hygiene practises in hospital, an area in which compliance is poor, in an effort to identify factors affecting nurses' behaviour associated with hand hygiene [191]. They identified barriers both to current hand hygiene practise and to implementing a new electronic monitoring system for hand hygiene. Barriers included; a lack of commitment to improve practise, lack of focus on long-term consequences and a tendency to focus on their individual performances as opposed to creating a high-quality network. As a result of this exploration of nurses' behaviours, implementation of this new system will now be an informed intervention with a higher chance of success.

Similarly, in order to implement changes in current prescribing practise for older people, it is necessary to identify prescribers' behaviour associated with the prescribing of inappropriate medicines. Further examination of the barriers and facilitators to these behaviours will allow for effective implementation of prescribing improvement interventions.

Behaviour change interventions can be modelled on any number of evidence-based theories that exist within health psychology [192, 193]. However, with so many to choose from, there is always doubt as to whether the model chosen fully accounts for the behaviour under investigation. A solution has been presented to this problem. An overarching theoretical framework, combining 128 constructs from 33 theories of behaviour change was developed by Michie *et al.* [194]. The resultant framework, known as the "Theoretical Domains Framework" (TDF) consists of 12 'theoretical domains' (See appendix V):

- Knowledge
- Skills
- Social/Professional Role and Identity
- Beliefs about capabilities
- Beliefs about consequences
- Motivation and goals
- Memory, Attention and Decision Processes
- Environmental Context and Resources
- Social Influences
- Emotion
- Behavioural Regulation
- Nature of the Behaviours

These domains serve as potential mediators of change. Using the TDF helps to define a behaviour and identify barriers and facilitators to that behaviour.

The TDF has been employed in a wide range of healthcare related research. An Australian study by Pitt *et al* has looked at why doctors refer, or do not refer, people with osteoarthritis to self-management programmes [195]. They found barriers to referral to be lack of awareness amongst GPs of the existence of these programmes and uncertainty as to the clinical benefit of them. Enablers to referral were awareness amongst patients of the value and availability of these programmes, and positive GPs' attitudes towards patient involvement [195]. In Finland, Amemori *et al* have studied why clinical guidelines recommending that dentists provide both tobacco abstinence and tobacco use cessation counselling to patients were not being implemented. They found that the environment in which the dentists work was inhibiting them from providing the counselling. They identified this as a potential target for interventions [196].

In the UK, the PROTECT study (PRescribing Outcomes for Trainee doctors Engaged in Clinical Training) investigated the prevalence and causes of prescribing errors made by junior doctors. As part of this study, Duncan et al used the TDF to explore the factors that influence junior doctors' prescribing behaviour [197]. They found seven domains to be likely mediators of change and using previously published methods [198], suggested several behaviour change techniques likely to be useful in an intervention study [197]. Similarily, in order to implement changes in current prescribing practice for older people, it is necessary to identify the processes leading to the prescribing of inappropriate medicines. Further examination of the barriers and facilitators to these processes will allow for effective implementation of prescribing improvement interventions.

The TDF was later expanded to 14 domains in 2012 by Cane *et al* [199]. Their study aimed to identify the optimal number of domains and domain labelling as well as to validate the contents of the domains and the TDF tool as a whole. In seeking the optimal structure for the TDF, they found that with their 14 domain version, explanatory and predictive power were increased making it a more useful tool for informing interventions. To date, the TDF has not been used to study the behaviours associated with PIP.

Once domains within the TDF are identified, they can be mapped to suitable intervention types using the 'behaviour change wheel', a previously published technique also developed by Michie *et al* [200] (See appendix VI). The behaviour change wheel consists of nine different intervention functions. The TDF domains

that are found to be relevant will determine which intervention functions would be suitable to change the behaviour in question. The intervention functions are;

- Training
- Restrictions
- Persuasion
- Incentivisation
- Environmental restructuring
- Education
- Coercion
- Enablement
- Modelling.

Each intervention function relates to several behaviour change techniques (BCTs) which are the specific activities needed to carry out the intervention [201].

The aims of this study were;

(1) To explore hospital doctors' perceptions as to why PIP occurs using a phenomenological approach with a constructivist paradigm.

(2) To identify the barriers to addressing the issues identified, thus identifying potential targets for intervention, and

(3) To determine which intervention types would be best suited to minimizing PIP form a prescriber perspective.

3.2 Methods

3.2.1 Sampling

In Ireland, there are three types of hospitals; (1) public hospitals, owned and funded by the Health Service Executive (HSE), (2) voluntary hospitals, which are run by voluntary/private boards who receive money from the government to provide health care services and (3) private hospitals which receive no state funding. Hospitals were purposively selected to ensure that a range of different hospital types were included in the study-Large HSE, small HSE, large voluntary and small voluntary. Doctors were then purposively selected within each hospital.

A sampling matrix (**Figure 3.1**) was designed to ensure our participant sample was representative of doctors prescribing for older people in the hospital setting and represented doctors working in both geriatric medicine and in general internal medicine. The matrix ensured that an equal number of doctors of each grade, both from geriatrics and general medicine, and from each hospital were interviewed.

	Intern	SHO	Reg/SpR	Consultant
Large HSE Hospital (CUH)	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric
Small HSE Hospital (Mallow/Nenagh)	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric
Large Voluntary Hospital (MUH)	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric
Small Voluntary Hospital (St. John's Limerick)	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric	1 x General 1xGeriatric

HSE = Health Service Executive. CUH = Cork University Hospital. MUH = Mercy University Hospital Cork. Intern = 1st year qualified. SHO = Senior House Officer (next stage after intern). Reg/SpR = Registrar/Specialist Registrar.

Figure 3.1 Sampling matrix

The chosen hospitals, in the Munster region of Ireland, were contacted and asked if they would take part in the study. The chief hospital pharmacist was the point of contact in all hospitals, and approached hospital doctors to explain the study objectives. They were provided with a written description of the study's background, aims and methods, and were asked to pass this information to hospital consultants. Consultants were asked if they would make themselves and their team available for a 25-30 minute one-on-one interview. This was then followed up with an email within one week of the initial contact with the chief pharmacist. Consultants willing to participate approached each member of their team informing them of the study and provided details of those team members who were willing to participate. Doctors were excluded if they were working in surgery, were involved in research related/similar to this study (currently or in the past), or had a pharmacy degree prior to undertaking their medical training.

3.2.2 Data collection

A phenomenological approach with a constructivist paradigm was the methodology deemed suitable. The method of data collection was semi-structured interviews. Interview topic guides were formulated based on the TDF (see appendix VII). Using the TDF helps to define a behaviour and to identify barriers and facilitators to that behaviour. The original 12 domain TDF was used [194], due to its proven track record and use in similar studies [194-197]. The interview schedule was then evaluated by pilot study with three health-care professionals and amended accordingly.

Semi-structured interviews were the preferred method of data collection as it is well established that semi-structured interviews penetrate sufficiently into the core of a subject and elicit more meaningful responses from participants [202].

The purpose of the topic guide was to explore the 12 domains of the TDF, while also allowing participants to speak freely, unlimited by strict questions. It has been shown that interviews based on the TDF elicit responses from participants that would not otherwise be reported [203].

Participants were briefed about the study and reassured that all interviews would be anonymized. Demographic details were collected before the interview, including: grade; gender; number of years working as a doctor; his/her current specialty; details of any specific training in geriatric medicine they may have received and university attended. Interviews were audio-recorded and later transcribed verbatim. They were also asked some general questions regarding their knowledge and awareness of PIP.

Interview locations included a private hospital office used for various research projects, consultants' private offices, hospital canteens and doctors' lounges. All locations were on hospital campuses to minimise disruption to participants.

3.2.3 Data Analysis

A similar approach adopted by Duncan et al [197] was followed for this study as a similar behaviour was being investigatetd i.e. prescribing. All transcripts were entered into QSR NVivo® Version 10 to facilitate analysis. Analysis was conducted in 2 phases. Phase 1 was a familiarisation phase, where transcripts were read and re-read to ensure that researchers were familiar with the entire content of all transcripts [204]. In phase 2, conventional content analysis [205] was conducted, independently by two researchers. In conventional content analysis, the researchers identify themes within the transcripts, and code all subsequent texts to these themes as they arise. Findings were compared and differences resolved through further discussion, analysis and consensus [206].

Directed content analysis [205] was then employed to apply the TDF and identify relevant domains. In directed content analysis, unlike conventional analysis, texts are coded to a pre-defined list of domains or research findings. A domain was deemed relevant if text from the interview transcripts was frequently coded into that domain *and* participants suggested that constructs within the domain were an influencing factor in PIP (see appendix VIII for screenshots of the process). Again, the domains identified as relevant were agreed upon by two researchers.

The behaviour change wheel [200] was then used to identify intervention types that would be suitable, given the domains identified.

It was decided to use two forms of content analysis to ensure that all relevant themes were identified. For the purposes of the study, and to identify domains to be targeted in a future intervention, the directed content analysis was to be the primary data source. The conventional content analysis was to be used to identify other, less critical areas of interest that may arise but which did not fit directly into the TDF.

Ethics approval for this study was sought from and granted by the Clinical Research Ethics Committee in University College Cork, Republic of Ireland (see appendix IX).

3.3 Results

All doctors approached to take part, did so and a total of 22 interviews were conducted.

Four hospitals took part i.e two HSE and two voluntary (one large and one small of each), as well as all grades of doctor (**Table 3.1**). Thematic saturation was reached after 18 interviews, another four were carried out to ensure no new themes were emerging, as per the Francis method [207].

Table 3.1: Participant Characteristics

Hospital	Total No. of participants from each	Grades of participants	Total No. of participants working in geriatrics	Sex
Large HSE	6	2 X Intern 2 X SHO 2 X Reg 1 X Consultant	2	3 X Male 3 X Female
Small HSE	5	1 X Intern 2 X SHO 1 X Reg 1 X Consultant	3	3 X male 2 X Female
Large Voluntary	6	1 X Intern 2 X SHO 1 X Reg 2 X Consultant	3	4 X Male 2 X Female
Small Voluntary	5	1 X Intern 1 X SHO 1 X Reg 1 X Consultant	2	2 X Male 3 X Female

HSE= Health Service Executive. Intern= 1st year as qualified doctor. SHO= Senior House Officer (Next stage after Intern). Registrar (Reg)= Next stage after SHO

As mentioned above, the topic guide used for the interviews was designed to explore the domains of the TDF. However it also included some questions designed to provide a cross- sectional picture of doctors' awareness of PIP and prescribing in general for older patients. Some points of interest from these questions follow.

(1) When asked to estimate what they thought the prevalence of PIP in hospitals was, the vast majority guessed above 50%. (2) When asked if they thought it was a problem that needs corrective action, all but one concurred (3) When asked where they thought PIP might be most prevalent i.e. in primary, secondary or tertiary care, 14 doctors felt it was highest in primary care, (where it has actually been shown to be lowest [11, 13, 17, 163, 164]). (4) When asked to rate their confidence in

prescribing for older patients on a scale of 1-10 (10 being the most confident), over half placed it at between 5 and 6. These were all interns (house officers) and senior house officers (SHOs). (5) When asked if they were aware of any screening tools to aid in prescribing for older patients, only the consultants were able to name the common ones. The other participants, for the most-part had heard of them but had no idea what they were.

Approximately half the doctors interviewed were, at time of interview, working in geriatric medicine (**Table 3.1**), with the remaining working in other medical specialties or in general internal medicine. The majority of doctors in geriatrics mentioned, without prompting or direct questioning on the matter, that prescribing within geriatrics was in general, far more appropriate than in other medical specialties they have experienced. There was a common trend within this group that more exposure to geriatricians would be of great benefit to prescribing in older patients, and this was also echoed by doctors not currently in geriatric medicine.

3.3.1 Conventional content analysis

Following familiarisation, and open coding, four over-arching themes, contributing to PIP were identified. They were;

- More education required in the area of geriatric pharmacotherapy.
- Prescribing environment is conducive to PIP,
- Poor information technology (IT) infrastructure,
- Lack of collaboration between levels of care.

3.3.2 Directed content analysis

To identify relevant domains in the TDF that could be targeted in an intervention, directed content analysis was employed. In all, five domains were identified as relevant;

(i) Environmental context and resources

(ii) Memory/attention and decision processes

(iii) Knowledge

(iv) Skills

(v) Social influences

These same domains were identified from both the geriatricians' interview transcripts and those not working in geriatric medicine. Behaviour regulation and beliefs about capabilities were also identified at an early stage. However, although purported to in some interviews, they were not indicated as being a significant contributory factor in PIP. How each of the five relevant domains were represented is presented below. Knowledge and skills are presented together since participants made little distinction between the two. More quotes supporting the different domains are presented in **Table 3.2.**

3.3.3 Environmental context and resources

The environment in which doctors prescribe was noted throughout the interviews, with interviewees reporting that the circumstances in which they prescribe are conducive to PIP. In particular, their workload, being interrupted while writing prescriptions and a lack of supportive IT infrastructure within their working environment, were considered conducive to PIP. They identified the

multidisciplinary team structure as a definite facilitator to appropriate prescribing, but indicated that its impact is attenuated by inefficient use of the resources within this team.

"That's a major problem. What you want to do when you're writing out a drugs kardex [prescription chart], is to be on your own, to be left alone, for five minutes while you just write out the thing. But it's actually an ideal opportunity for anybody who wants a piece of you for advice or whatever, (…..) nobody respects that at all" **Site 1, interview 6 (Intern)**

A theme evident throughout many of the interviews was that of limited resources available, with particular emphasis on the lack of IT infrastructure. Interviewees noted that improvements and developments in the IT infrastructure could lead to much safer and more appropriate prescribing. Many doctors emphasised that prioritising improvement initiatives around IT infrastructure could have the most significant impact on prescribing quality.

"Part of the reason (for PIP) *is there isn't a very good interface between the electronic systems that they* [General practitioners (GPs)] *use and the electronic systems that we use. So in an ideal world the GPs should be able to electronically send in all up to date information."* **Site 3, interview 2 (Consultant).**

A further issue raised by the interviewees, was the team support within the hospital environment. Particularly, the hospital pharmacist was considered a useful team member and a reliable resource. However, interviewees felt that the pharmacist's input was not used to full effect, with many doctors not having regular pharmacist

input into the prescribing process. Some interviewees also noted that the way in which advice from pharmacists was communicated to the prescribers was important, with interviewees favouring face-to-face communication rather than written communication.

"…obviously it would be nice to think that every ward would have a pharmacist attached to it reviewing kardexes [prescription charts] *and educating (….) but there is a feeling that the pharmacist comes and writes a note for you, but it's not done face to face, and it actually is a bit antagonistic if anything (….) having 'post-its'* [notes] *stuck on things saying please review this, please review that. We all hate notes, everyone hates it, so I think that could be done better. So more pharmacy input, but more integrated pharmacy input"* **Site 3, interview 2 (Consultant)**

3.3.4 Memory/attention and decision processes

Participants referred to this domain in two contexts. Firstly, in conjunction with the high pressure environment in which they prescribe and their workload. This environment affects the attention they can give to each patient and their medicines. Their attention is not at the level it would otherwise be.

"Particularly in A&E [accident and emergency] *which is where you are doing the core prescribing, trying to determine what they should be on., making decisions about whether to hold things or not, and I mean there are four SHOs* [senior house officers] *trying to talk you, along with nurses and stuff"* **Site 1, interview 1 (Registrar)**

Secondly, several participants suggested doctors' decision-making and the processes surrounding it as a cause of PIP. There was a feeling amongst these participants that there is wide variation in practice amongst doctors, and that some do not go to the lengths required, or give sufficiently careful consideration to make an informed decision when prescribing.

"…when they come in, and they don't have a list of their medications, some people just inappropriately write down the dose that they think that they should be on or whatever, which often happens. Or a prescription of a patient that just came in on Sunday, had just the medications written with no doses at all (….) so if you're not going to write a dose you probably shouldn't write anything." **Site 1, interview 1 (Registrar)**

3.3.5 Knowledge/Skills

Although separated into two domains in the TDF, participants for the most part alluded to constructs within these domains as a single domain, and therefore these domains are reported together. Participants noted a lack of specific education and training in geriatric pharmacotherapy, and also a lack of communication of clinically relevant information with regards to older patients, such as which drugs to avoid. Interviewees noted that experiential learning is how their prescribing skills and knowledge of issues around prescribing in older people progress.

However they felt that this was not sufficient and that further structured training was required.

"I'd say if there was a monthly, or periodic review of the literature (…) to put out a newsletter or something, for medications that are found to be obsolete, medications that are found to be harmful, because we see a lot of people on medication that were used ten or twenty years ago and are no longer in the guidelines and no longer the current practice (…) I think that would be a good idea." **Site 2, interview 2 (Registrar)**

"I don't think there is enough training for prescribing in older patients. There is no distinction between older patients and the general adult population in the training. You just learn it from practice." **Site 4, interview 2 (Registrar)**

Patient education was also considered important.

"And even when they [the patients] *bring a list, their knowledge of those meds is not good. And the patient education of their own drug therapies is fairly poor. Community wise, nationwide, there is a big area that needs to be addressed in terms of patient education"* **Site 2, interview 1 (Consultant)**

3.3.6 Social influences

Participants were specifically asked about outside influences that may affect their prescribing and perhaps increase the risk of PIP. The majority of doctors admitted that patients and patients' families can influence their

prescribing, to the point where the doctor may prescribe a drug he/she is not completely comfortable with.

*"As a doctor sometimes, you feel that you have to do something, you get pressurized by either nursing staff, relatives or patients. You have to give them something. So you end up giving something that you are not 100% happy with. "***Site 2, interview 2 (Registrar)**

Most interviewees did say however that they didn't think these choices were putting their patients at any risk due to these choices after weighing the risks and benefits and that the quality of life was a major deciding factor.

"I would like to think that we never prescribe something that we know is wrong or don't prescribe something that we know is right, even if the family has concerns, I do think we can stand our ground and document their concerns and do it (…) I think we are always just thinking about the patient's quality of life (…) but there's no doubt it sways you where it's a grey area" **Site 3, interview 2 (Consultant)**

Table 3.2: Supporting quotes from interviews

TDF Domain and intervention types identified as suitable by the behavior change wheel	Supporting quotes
Environmental context and resources **Behaviour change wheel interventions identified:** -Environmental re-structuring -Persuasion -Incentivisation	*"I do think though, it's a tough job, it really is very tough, you're just flat out busy all the time, I think a lot of times you're just transcribing things you just go into auto pilot and you transcribe things that have already been prescribed and you don't question it."* **Site 3, interview 1 (Intern)** *"We should have open access computers on every ward for resources including BNFs and other sorts of policy documents, antimicrobial policy and other things you use all the time. And these are all barriers, if you're unsure about checking the medication, these are all barriers that will put a lazy person off am, checking it. I think it's really important that we have better access to IT on every ward. It's really terrible at the moment."* **Site 1, interview 6 (Intern)** *"I think it* [improved IT inifrastructure] *is a resource that would be potentially brilliant for drug and prescribing management, in general. How could I give you a better example of that now……I think let's say in community, in retail pharmacy, there are platforms available which off the bat* [straight away]*, will flag drug-drug interactions, as you fill a script, and it's up to the pharmacist to look at it. We don't have anything like that, and it would be so easy."* **Site 1, interview 6 (Intern)** *"In New Zealand we had a pharmacist for every team in the hospital who used to go around and check all the meds and they were very much part of the medical team and we took a lot of advice from them because they had more time to go through them* [the medicines prescribed]*. I know like the culture here is kind of, that we* [prescribers] *are in charge of meds, but that was one thing that was brill, and it wasn't just a green thing on the front of the chart, they would go through every admission, which was a big job, but they would go through every patient and go on the ward round, and they would have a medical idea of why the patient was in and recommend changes to the medications. I thought that was very good. The team didn't have to take the advice. Pharmacists are better at that kind of thing so I think that would be a really good idea"* **Site 1, interview 1 (Registrar)** *"I think that actually, I do think pharmacists have helped me an awful lot this year. Like things like pointing out drug interactions that you mightn't have noticed (….) definitely find the pharmacist really helpful so I don't mind them ringing me and their notes are great on the kardexes [prescription chart] and stuff. And it's especially helpful if there's something the patient can't remember".* **Site 4, interview 6 (Intern)** *"Well we don't have clinical pharmacy involvement here, which hopefully it's going to start and that's a great thing you know it improves our prescribing overall."* **Site 4, interview 3 (Consultant)**

Table 3.2 Contd

Memory/attention and decision processes **Behaviour change wheel interventions identtified:** -Enablement -Modelling	*"You know sometimes you're writing three or four pages of a drug kardex, and to look at every possible interaction, you know you'd see the common things but the less common things get overlooked all the time."* **Site 2, interview 3 (SHO)** *"….some people just believe everything the patient says at face value without ever really investigating whether or not they actually know what they are talking about"* **Site 4, interview 1 (SHO)** *"I think you have to be more thoughtful prescribing for elderly patients and I think a lot of people just do it without taking enough care and stuff like that, you know you have to know what you're prescribing and you do have to be aware of any interactions."* **Site 3, interview 2 (Consultant)**
Knowledge and skills **Behaviour change wheel interventions identified:** -Enablement -Modelling	*"It's a different knowledge set. And it's difficult you know because there isn't a huge amount of data out there, or its not communicated to us very well, I mean we all hear about the randomised controlled trials when new drugs come out, we get info* [information] *about that but we don't really hear much like, on grand rounds you know, what meds are good or bad in elderly people"* **Site 1, interview 5 (Registrar)** *"….as an undergrad, students don't have a tenth of the teaching that they should have, all doctors of all levels will openly put their hand up and say, as an undergrad, they didn't have the teaching so most definitely they should be an increase in what they are teaching in clinical pharmacy, they should have a huge amount more time at undergraduate level for that because it's such a dangerous occupation you know, prescribing, something has to be done about it"* **Site 3, interview 1 (Intern)** *"I think we do need a lot more patient education, I think we do need the patients, not only going home, not only having a prescription, but they have a detailed patient education leaflet, documenting all the drugs they are on, and their purpose, frequency and duration."* **Site 2, interview 1 (Consultant)**
Social influences **Behaviour change wheel interventions identified:** -Restrictions -Persuasion	*"There is no doubt that we would come under pressure to prescribe anti-depressants or sleeping tablets from the family members, not just the person and you have to resist that if you think it is inappropriate but you know, the fact that you have to resist it means that sometimes you probably are swayed by it. And similarly there may be a medication that you may be thinking of prescribing and the family say absolutely no, or have huge concerns about it you know if you are iffy about it, that might be enough to dissuade you."* **Site 3, interview 2 (Consultant)** *"I'd start with education actually, but its educating patients as well you know. There's a notion out there you know that you go to the doctor, and the outcome of any consultation should be a prescription."* **Site 4, interview 4 (Consultant)**

3.3.7 Barriers to behaviour change

From the above analysis, it can be seen that the main barriers to appropriate prescribing are:

- An environment which is conducive to sub-optimal prescribing

  -Interruptions, lack of IT infrastructure, distracting environment, all combine to make it difficult for the prescriber to give the extra thought required to ensure the older patient's prescription is appropriate.

- Strained resources

  -Lack of targeted pharmacy input on the wards, poor collaboration between different levels of care due to busy schedules, and again lack of IT infrastructure.

- Lack of specific training

  -Not enough geriatric pharmacotherapy training, particularly for undergraduates. Prescribers feel ill-equipped to prescribe appropriately for older patients with multi-morbidities and associated polypharmacy.

- Poor patient education

  -Patients' knowledge of their own medicines is generally poor and they can often be reluctant to change long-term prescriptions. This can make adjusting medications difficult for the prescriber.

3.3.8 Behaviour change wheel

Having identified the domains within the TDF [194] that are relevant to PIP, the behaviour change wheel [200] was then used to identify intervention types that would be suitable to address these domains. According to the behaviour change wheel, the types of interventions that would be beneficial in the area of PIP are; training, environmental restructuring, restrictions, persuasion, incentivisation, modelling and enablement.

3.4 Discussion

This is the first study to use a theoretical approach to investigate issues associated with potentially inappropriate prescribing in older patients.

The responses to the general questions at the start of the interviews paint a clear picture. Doctors are aware that PIP is problematic in this age group. Their estimations of its prevalence were quite accurate. However they feel ill-equipped to deal with it and are poorly informed about the measures that already exist to deal with it, as illustrated by their widespread lack of awareness of the common screening tools for prescribing in older patients.

The consensus amongst all doctors (not just those in geriatrics) that increased exposure to geriatricians would be of great benefit is an important point. It is logical that guidance from experienced geriatricians would improve prescribing in older patients, but to hear it from practicing doctors, who have experienced prescribing within multiple specialties emphasizes this point. It is also of interest that the same TDF domains were identified from the transcripts of doctors working in geriatric

medicine as well as in other specialties. This is not surprising since doctors from all medical specialties are caring for more and more older patients currently, so the challenges these patients present are common to all who prescribe for them.

The domains in the TDF identified as relevant provide the details to the overall situation described above. It is well recognised that a doctor's workplace can be chaotic [208, 209], and so the emergence of 'environmental context and resources' was not unexpected. Improving the environment in which doctors prescribe is not an easy task. However, areas have been highlighted throughout these interviews that could be good starting points. For example, making better use of the resources available. In particular, the hospital pharmacist. Perhaps interventions designed to restrict interruptions to doctors while writing prescriptions. In addition, improved IT infrastructure would likely improve prescribing in older patients generally.

The domain of "memory/attention and decision processes" was clearly intertwined with the domain "environmental context and resources". Even with a calm prescribing environment free of distractions, prescribing is still a challenging exercise. The complexity of prescribing for multi-morbid older patients is well recognised. Aronson has identified the need for a wide range of skills and judgment when prescribing, and the increased challenges when dealing with a vulnerable population [210-212]. With the extra stresses the work environment brings the exercise of prescribing and correct therapeutic decision making becomes significantly more difficult. Doctors' indications that decision making processes, particularly when writing prescriptions, vary quite significantly between individuals is an important point to consider, and a possible target for intervention.

Providing an environment more conducive to appropriate prescribing will address this issue to some extent. However, the interviews also suggest that greater efforts are needed to standardize doctors' prescribing practices.

'Knowledge' and 'skills' were two clear areas that participants felt could be targeted, although for the most part they referred to these domains as one entity. The majority of interviewees expressed a desire for further training; those who did not were the most senior doctors i.e. hospital consultants. Most interviewees felt they did not receive adequate *specific* geriatric pharmacotherapy training as medical undergraduates. In addition, there was a perceived lack of communication of the salient therapeutic points from the research literature once they qualify. This is an area with significant potential for intervention in terms of feasibility. Pharmacists and clinical pharmacologists are ideally placed to address this issue and equip doctors with the necessary tools to prescribe for older patients. Restructuring the undergraduate medical curriculum is also required, with more emphasis on geriatric pharmacotherapy. It should be noted that while participants mostly referred to 'knowledge' and 'skills' as one and the same, they are in fact fundamentally different behavioural determinants and as such, require different interventional approaches. 'Knowledge' can be enhanced through increased education, whereas addressing 'skills' may require non-technical training, as reported by Gordon et al [185].

An unexpected result of the study was the emergence of the domain 'social influences'. Over half the participants, including the majority of consultants, said

that they would be, and/or have been influenced by the patient or their family to prescribe in a manner that could be deemed inappropriate, with several doctors using the term "*forced to prescribe*". Although most interviewees added that they still felt they weren't putting the patient at risk, the notion of a doctor feeling forced into a prescribing decision is worrying. Many interviewees referred to patient education as a solution to this. Dealing with patients' and families' demands, and being able to resist demands, is likely an important component of educational interventions going forward. Implementation of the model for delivery of this type of training in 'non-technical skills' proposed by Gordon *et al* [185] is warranted given the findings of this study.

The findings correlate well with the meta-synthesis in chapter 2, which found that some doctors feel restricted in terms of their abilities to prescribe appropriately due to a combination of factors such as pressure to please the patients, and fear of doing harm by changing a patient's medications [156]. Shared decision making with patients [213] should also be explored as a means to address this issue that doctors have identified as problematic. This would also counter-act the traditional paternalistic approach to prescribing which has previously been identified as problematic and contributory to PIP [180].

It should be noted that while doctors admitted to sometimes knowingly prescribing inappropriately, in certain circumstances, they were conscious of paying more heed to the patient's quality of life rather than the appropriateness of their prescriptions. This is an important consideration as these patients' therapeutic targets are often very different from those of younger adults.

This study has highlighted the specific barriers to change that exist in the area of PIP. The intervention functions identified through use of the behaviour change wheel correlate well with these barriers, in that, interventions based on environmental restructuring and training would certainly seem logical given that three of the four barriers identified fall under 'environment' or 'training'. We can be confident therefore, that an intervention informed by these techniques would likely be justified and beneficial.

To date, interventions that reliably counteract PIP in older patients are lacking. O'Connor et al [52] recently conducted a review which suggests 4 areas of intervention to counteract PIP in this population, namely comprehensive geriatric assessment, medication use review, prescriber education/audit/feedback and computerized prescriber order entry with clinical decision support. The evidence to support any of these interventions to prevent PIP in older patients is however weak. Prescriber education interventions to prevent PIP in particular drug classes have been shown to work, e.g. antibiotics, opioid analgesics and antipsychotics [52]. Whether prescriber education can minimize PIP in older patients in general is unknown.

Although the TDF domains were examined and presented individually, there is significant cross over between them. The environmental context has an impact on doctors' memory/attention and decision processes, as well as their ability to carry out basic skills. Similarly, doctors' particular skill sets may determine whether or not they are prone to social influences and whether they allow such pressures to affect their prescribing. Bearing in mind these cross overs between domains, it is

highly probable that an intervention to address PIP will have to be multi-faceted. One of the intervention types identified by the behaviour change wheel is unlikely to result in a significant improvement if implemented in isolation. A combination of intervention types however would be justified and would likely have a higher chance of success.

3.5 Limitations

Much of the responsibility for recruitment of participants for this study laid with a third party i.e the hospital pharmacist. While it was useful to have a person known to the medical staff to introduce the project, it is preferable that the researcher(s) claim responsibility for recruitment when using qualitative methodologies.

Whilst the sampling matrix was used to ensure inclusivity within the hospital setting, this study therefore reflects the barriers encountered by hospital doctors, and is not generalizable to primary care.

The sample size of 22, although acceptable for qualitative research, is small, and as with all qualitative research, is not generalisable.

3.6 Conclusion

Doctors are aware that PIP in older patients is a real problem that needs solutions. The current study indicates that the causes are a combination of environmental and social factors, compounded by doctors' lack of specific training and education in geriatric pharmacotherapy. This study has identified key areas for targeting of intervention studies in the future, as well as intervention types that should be used.

4. Use of an e-learning educational module to better equip doctors to prescribe for older patients - A randomised controlled trial

Chapter description

Amongst the findings from Chapter 3, it was reported that doctors feel they do not receive enough specific geriatric pharmacotherpay education as undergraduates. They expressed a desire for this teaching to be delivered in such a way as it could be completed in their own time. Therefore, an educational intervention was developed which delivered on this and the impact of it on prescribers' knowledge and confidence with regards to prescribing for older patients was explored by randomised controlled trial.

The work of this chapter is currently under review for publication in the British Journal of Clincal Pharmacology.

4.1 Introduction

Earlier chapters of this thesis have highlighted the negative impact PIP in older patients is having on healthcare systems both in Ireland and abroad [11, 12, 15, 17, 214]. Older patients' susceptibility to PIP has also been described [187, 188]. The difficulty with prescribing for older patients stems from a lack of evidence of the effectiveness of medicines in the multi-morbid older patient [52], as well as altered pharmacokinetic and pharmacodynamic properties of some drugs when consumed by older patients [53]. Hence, the older patient population is significantly different from the younger adult population with regards to dose selection for a wide variety of drugs.

Recent investigation of prescribing attitudes and behaviour indicate that doctors feel there is insufficient distinction made between the two adult populations i.e younger and older adults during their undergraduate education, and that doctors do not receive enough education and training in geriatric pharmacotherapy either at undergraduate or postgraduate levels [215], as highlighted in Chapter 3. As a result, doctors may lack the confidence to make decisions as to the appropriateness of pharmacotherapy when dealing with older patients [216, 217]. Recently published research also indicates that recently graduated doctors feel that supplementary training, delivered in a way that would allow them to complete it in an on-line format and in their own time would be of benefit [215].

The qualitative research described in Chapter 3 exploring doctors' beliefs about the causes of PIP, indicates several possible areas for intervention [215]. Not surprisingly, online educational interventions and supplementary training are among them. Educational interventions have had moderate success in various clinical disciplines in the past, and randomised controlled trials have shown that such interventions significantly reduce the amount of inappropriate prescribing [107, 108]. The overall evidence as regards efficacy of educational interventions has been somewhat mixed [52, 103, 104]. However, many of the previous studies in the past have not been well informed by prior qualitative research or have not utilised technology to make educational tools and resources more convenient to the participants with a view to enhancing efficacy [110-112]. Also, most of the previous studies have focused only on single drug classes, rather than prescribing in general in the target population [106-108].

Previous studies indicate that online educational, 'or 'E-learning', interventions are at least as effective as standard educational techniques [218-220], and have shown promise in the area of paediatric prescribing [221]. As stated in the literature, it is unlikely that any one form of education will ever suffice, and a combination of complementary techniques will very likely be required for maximum efficacy [218].

The aim of this study is to determine if an online educational module, focused on geriatric pharmacotherapy improves doctors' prescribing knowledge, as well as prescribing confidence as applied to older patients.

4.2 Methods

4.2.1 Study design

The impact of the intervention on doctors' knowledge and confidence with regards to prescribing for older patients was measured using a non-blinded randomised controlled trial.

4.2.2 Intervention

For the online module, a licence to use the 'Standard Computerised Revalidation Instrument for Prescribing and Therapeutics (SCRIPT)' tool developed by NHS Health Education West Midlands, University of Birmingham and OCB Media in the UK was obtained. This is a comprehensive doctor training tool utilised in the UK which covers all aspects of prescribing, including a specific module for prescribing in older patients (See appendix X for screenshots of the module). Areas covered in the older person prescribing module include drug-drug interactions, pharmacokinetics, pharmacodynamics, adverse drug reactions and appropriateness of prescribing. This interactive module is designed to be completed in 1-2 hours and has been peer-reviewed by experts in geriatric pharmacotherapy. No comparable educational tool is currently available to doctors in the Republic of Ireland.

Three assessments were created and marking schemes agreed upon by a consultant physician in geriatric medicine and 2 clinical pharmacists (Appendix XI). Each assessment consisted of 10 multiple choice questions (MCQ) (20 marks) followed by 5 case studies (30 marks). The case studies in each assessment tested participants' knowledge of prescribing appropriateness in older patients, requiring them to identify specific issues with regard to the patient's prescription. At the end of each

assessment, the participants were asked some questions about their confidence levels when prescribing for older patients, their opinions of the training they had received so far, their knowledge of tools to aid in prescribing for older patients and their opinions of PIP in older patients.

At baseline, both groups (control and intervention) completed the first assessment. Participants in the intervention group were then given access to the Script module for 4 weeks. After this time, both groups completed the second assessment. The third and final assessment was completed by both groups after 12 weeks.

4.2.3 Recruitment

Non-consultant hospital doctors (NCHDs) of all grades i.e house officers (interns), senior house officers (SHOs) and registrars were recruited from 6 public hospitals within the Health Service Executive (HSE) Southern Region in Ireland between January and April 2015. Exclusion criteria were: having a pharmacy degree; history of working in the pharmaceutical industry; working as a consultant doctor. It was calculated that a sample of 78 participants was required to provide 90% power to detect a 20% difference in mean test scores post-intervention. To allow for an expected 35-45% attrition rate from baseline to 12 weeks, a sample of 146 was obtained.

Sample size calculation for a continuous endpoint

Standardised difference = Difference to detect / anticipated standard deviation = 10 marks (20%) / 13.5 (SD reported from similar study) [221]

=0.74

Table 4.1: Sample size table for continuous variables showing number of patients required per arm

Power	Standardised difference								
	0.55	**0.6**	**0.65**	**0.7**	**0.75**	**0.8**	**0.85**	**0.9**	**0.95**
0.8	53	45	39	33	29	26	23	21	19
0.9	71	60	51	44	**39**	34	31	27	25

With a standardised difference of 0.74, and requiring 90% power, 39 patients are required per arm, 78 in total. To allow for a max of 45% attrition, (78 / 55) X 100

= 140 participants required in total.

A computerised random number generator was used to allocate participants to control or intervention groups. Stratified randomisation was used to ensure even distribution of hospitals, grade of doctor (intern, SHO and registrar) and area of practice (medical, surgical and geriatrics) within each group.

4.2.4 Data analysis

The primary outcome measure was prescribing skill measured by the total correct responses in each assessment. Each assessment was marked out of 50, with 20 marks available for the multiple choice questions, and 30 marks for the case studies. Secondary outcomes were doctors' confidence levels with regards to prescribing for older patients as well as their opinions on the training they had received to date, their knowledge with regard to common screening tools for PIP

and their opinions as to what should be done to address the issue. The latter was treated as qualitative survey data and analysed accordingly through content analysis.

The researcher marking the assessments and performing the analysis was blinded to the allocation group of the participants during this process. To analyse test scores, the Student's t test was used. Data were analysed using IBM SPSS Statistics (version 22).

The Consolidated Standards of Reporting Trials (CONSORT) guidelines were applied during design, implementation and reporting of the trial [222] (Appendix XII).

Ethics approval was sought from and granted by the Clinical Research Ethics Committee, University College Cork (Appendix XIII). The trial was registered with the United States National Institutes of Health (NCT02405975) https://clinicaltrials.gov/show/NCT02405975

4.3 Results

As per the CONSORT guidelines, **Figure 4.1** shows the flow of participants through the trial. Seventy participants were randomised to the control group, of which 39 completed the 12 weeks. Seventy six were allocated to the intervention group, of which 41 completed the 12 weeks.

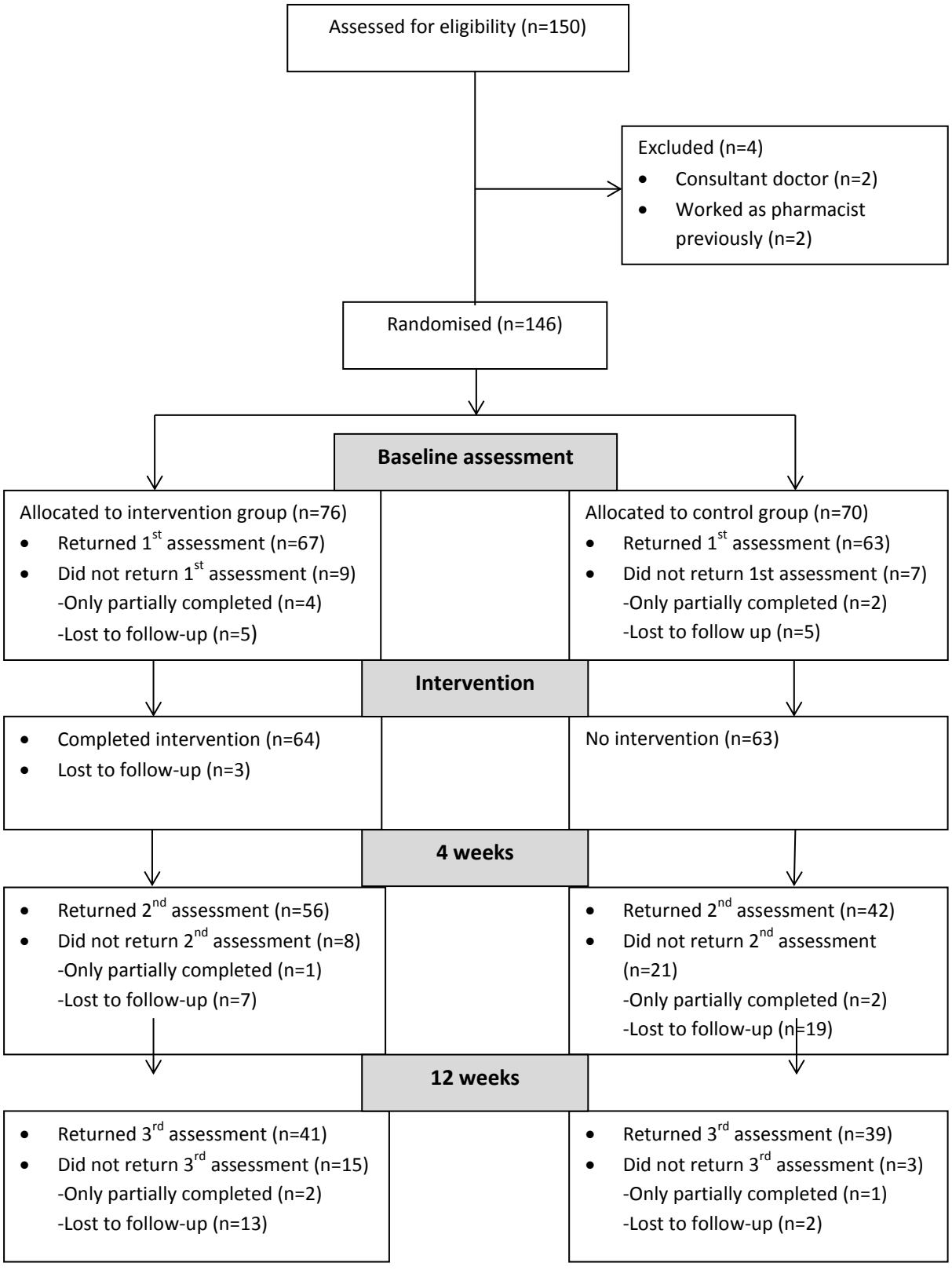


Figure 4.1: Flow diagram of participants through the trial

Table 4.2 shows the participant characteristics of each group. Stratified randomisation with a random number generator ensured even distribution of hospital, grades of doctor and specialist areas in each group.

Table 4.2: Participant characteristics of control and intervention groups

Control			
Hospital	**Grade**	**Area**	**Total**
1	Intern (n=12) SHO (n=7) Reg (n=9)	Medicine (n=11) Geriatrics (n=10) Surgery (n=7)	28
2	Intern (n=2) SHO (n=2)	Medicine (n=2) Geriatrics (n=2)	4
3	Intern (n=5) SHO (n=7) Reg (n=3)	Medicine (n=4) Geriatrics (n=6) Surgery (n=5)	15
4	Intern (n=1) SHO (n=2) Reg (n=2)	Medicine (n=2) Geriatrics (n=2) Surgery (n=1)	5
5	Intern (n=2) SHO (n=2) Reg (n=2)	Medicine (n=3) Surgery (n=3)	6
6	Intern (n=3) SHO (n=4) Reg (n=5)	Medicine (n=5) Geriatrics (n=4) Surgery (n=3)	12
		Total	**70**
Intervention			
Hospital	**Grade**	**Area**	**Total**
1	Intern (n=10) SHO (n=12) Reg (n=11)	Medicine (n=12) Geriatrics (n=10) Surgery (n=11)	33
2	Intern (n=1) SHO (n=3) Reg (n=2)	Medicine (n=3) Surgery (n=3)	6
3	Intern (n=5) SHO (n=6) Reg (n=1)	Medicine (n=4) Geriatrics (n=3) Surgery (n=5)	12
4	Intern (n=2) SHO (n=1)	Medicine (n=1) Surgery (n=2)	3
5	Intern (n=2) SHO (n=1)	Medicine (n=2) Geriatrics (n=1)	3
6	Intern (n=6) SHO (n=5) Reg (n=8)	Medicine (n=7) Geriatrics (n=5) Surgery (n=7)	19
		Total	**76**

There was no significant difference between control and intervention group scores at baseline (p=0.071) and the data across both groups was normally distributed with minimal skewness (skewness = 0.087), see **Figure 4.2**.

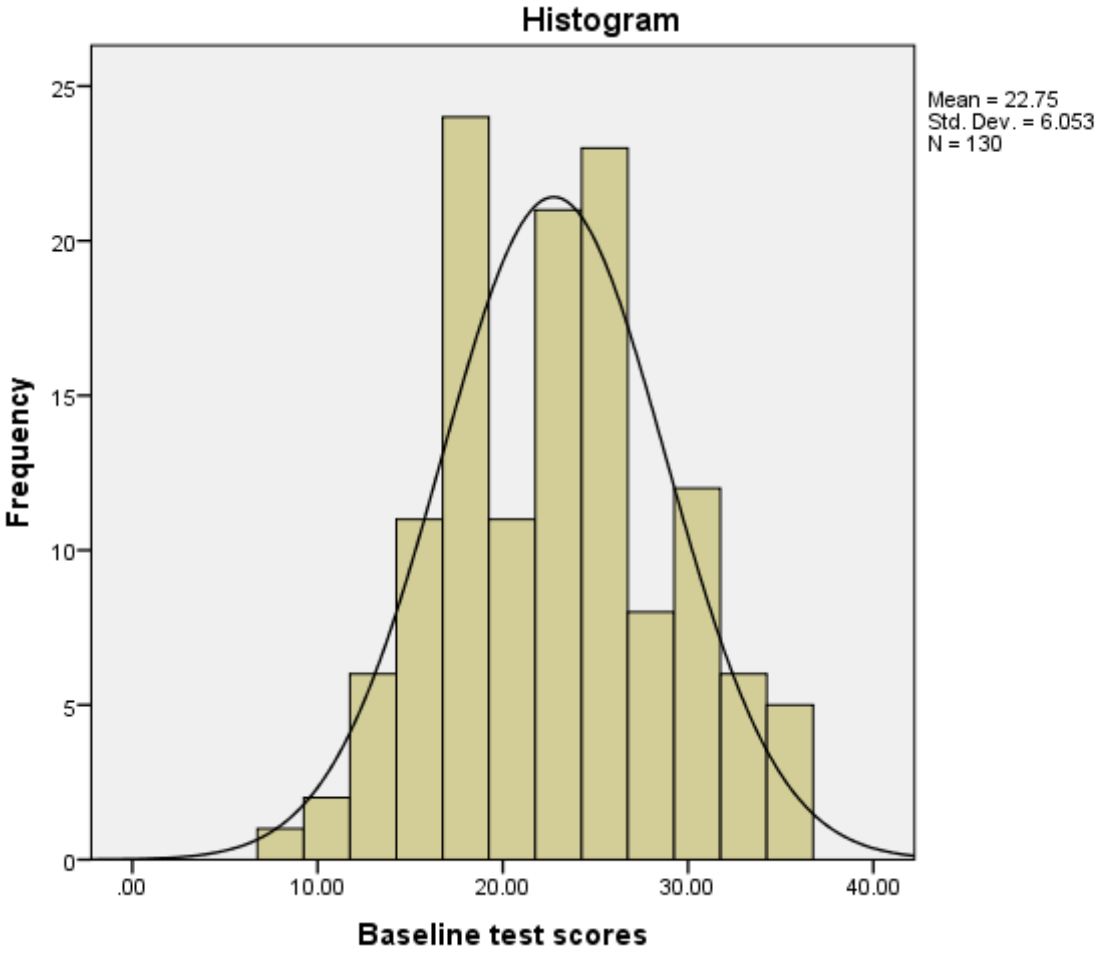


Figure 4.2: Distribution of test scores across both groups

Table 4.3 shows the baseline and post-intervention total scores for the assessments. A significant difference was seen between the groups at 4 weeks post-intervention, with the intervention group scoring an average of 11 marks higher than the control group, which equates to a 22% difference ($p<0.0001$), and a 24% improvement from their *own* baseline score ($p<0.0001$ using paired t-test for within group analysis). This significance was maintained at 12 weeks. There was no significant difference in scores within the control group between baseline and the 12 week assessment. There was no significant difference in scores at any time-point between interns, SHOs and registrars, or between doctors working in internal medicine, geriatric medicine or surgery. Interns improved the most between baseline and 4 week post-intervention with a mean difference of 7.2 marks, however this was not significantly better compared to SHOs and registrars (interns versus SHOs $p=0.804$, interns versus registrars $p=0.874$ using paired t-tests for within group analysis).

Table 4.3: Scores from control and intervention groups for each assessment

Assessment	Control group	Intervention group	p value (independent two-tailed t test)	95% Confidence intervals of the difference
Baseline Mean marks out of 50 (SD±)	23.74 (5.88)	21.82 (6.1)	0.071	(-4.00 , 0.17)
4 weeks post-intervention Mean marks out of 50 (SD±)	23.12 (5.93)	33.67 (5.99)	<0.0001	(8.13 , 12.97)
12 weeks post-intervention Mean marks out of 50 (SD±)	22.88 (4.48)	32.63 (4.59)	<0.0001	(7.72 , 11.76)

Table 4.4 shows the breakdown of scores for the multiple choice questions and the case studies in each assessment. There was no significant difference between control and intervention groups at baseline in the multiple choice questions or case studies (p=0.60 and 0.11 respectively). A significant difference was detected between the groups at 4 weeks post-intervention for both sets of questions, with the intervention group scoring an average of 4.65 marks higher than the control group in the MCQs, i.e a 23% difference ($p<0.0001$), and a 25% improvement from their *own* baseline score ($p<0.0001$ using paired t-test for within group analysis). This significance was maintained at 12 weeks. In the case studies, the intervention groups scored an average of 5.71 marks higher than the control group i.e a 19% difference ($p<0.0001$) and a 23% improvement from their *own* baseline score ($p<0.0001$ using paired t-test for within group analysis). There was no significant difference in scores within the control group between baseline and the 12 week assessments.

Table 4.4: Breakdown of scores for multiple choice questions and case studies

Assessment	Control group	Intervention group	p value (independent two-tailed t test)	95% Confidence intervals of the difference
MCQs				
Baseline MCQ Mean marks out of 20 (SD±)	10.76 (3.26)	10.46 (3.19)	0.60	(-1.42 , 0.82)
4 week MCQ Mean marks out of 20 (SD±)	10.71 (3.02)	15.36 (2.91)	<0.0001	(3.44 , 5.84)
12 week MCQ Mean marks out of 20 (SD±)	10.92 (3.52)	14.93 (3.33)	<0.0001	(2.48 , 5.53)
Case Studies				
Baseline Case Studies Mean marks out of 30 (SD±)	12.98 (5.43)	11.36 (5.86)	0.11	(-3.58 , 0.35)
4 week Case Studies Mean marks out of 30 (SD±)	12.60 (5.68)	18.31 (5.64)	<0.0001	(3.42 , 8.01)
12 week Case Studies Mean marks out of 30 (SD±)	11.96 (5.25)	17.70 (5.50)	<0.0001	(3.34 , 8.13)

At baseline, when asked to choose a statement best describing their confidence with regards to prescribing for older patients, 40% of participants in the intervention group, and 45% of participants in the control group chose 'not confident at all', with only 3% and 9% respectively choosing 'confident'. When asked the same question at 4 weeks post-intervention, only 16% of participants in the intervention group rated themselves as 'not confident at all' with 34% choosing 'confident'. Figures in the control group remained much the same as baseline ('not confident at all'=42%, 'confident'=12%). When asked for their opinions on the

geriatric pharmacotherapy training they had received prior to this study, 50% reported '*I did not receive sufficient training in geriatrics. I acquired, or am acquiring the necessary skills through practice, but feel there needs to be supplementary training also'*. Participants were asked if they ever use tools such as the Beers criteria [63, 64, 66] or STOPP/START criteria [69, 70] to aid with prescribing optimisation in older patients. 60% were unaware of the Beers criteria and 55% were unaware of the STOPP/START criteria. Finally, participants were asked for their own opinions as to what specifically would benefit prescribing in older patients and would address PIP in older patients. Content analysis of the answers revealed three over-arching themes:

(i) Supplementary training in Geriatric Medicine with more pronounced distinction made between older patients and the general adult population

(ii) Improved IT support in terms of transfer between levels of care

(iii) Increased communication between the levels of care i.e GPs, hospitals, pharmacies and nursing homes.

4.4 Discussion

This study has shown that a short e-learning module can significantly improve doctors' prescribing skills and prescribing confidence with regards to older patients. Furthermore, this is a sustainable improvement as shown by the scores after 12 weeks. The low scores in both groups at baseline, and low scores of the control group at each time-point, indicate that prescribing for older patients is indeed a challenging task for NCHDs. This is not just true for interns, who have been the focus of some recent sub-optimal prescribing studies [209, 223, 224], but for all NCHDs, in all areas of practice. With more and more doctors from every specialist area treating older patients on a day-to-day basis, these results illustrate the extent of NCHDs' limitations with regard to geriatric pharmacotherapy. Despite this, it is encouraging that an easy-to implement intervention such as this can significantly alter junior doctors' level of knowledge of geriatric prescribing for the better in a relatively short period of time.

Historically, studies such as this have not been followed up with research demonstrating a translation of these improved skills into actual improved patient outcomes [225]. While this study did not aim to demonstrate this, it is encouraging to note the significant improvement in participants' scores in the case studies. These cases were taken from real-life patient records and are therefore a good representation of the doctors' prescribing skill in actual clinical cases. Our data show that the intervention not only enhanced the participants' knowledge base, but also their decision making and overall prescribing skills.

The present study also shows an improvement in the participants' self-reported confidence levels with regards to prescribing for older patients after the intervention. Thirty four percent of doctors who completed the e-learning module reported feeling confident in their skills, compared to just 3% before the intervention. The low test scores in both groups at baseline correlate well with the finding that half of all participants felt they did not receive enough training in geriatric pharmacotherapy as undergraduates. This is compounded by the fact that over half of participants had never heard of the Beers criteria or the STOPP/START criteria, two well established tools for detecting potentially inappropriate prescribing in older patients. Participants' desire for supplementary training, improved IT support and increased communication between the levels of care further highlight the deficiencies that currently exist in the training and practice of doctors in relation to geriatric pharmacotherapy.

Given the multiple factors that contribute to PIP in older patients, future strategies to minimize PIP will require a multi-faceted approach. This study shows that well-structured, accessible prescriber education interventions such as this have a significant role in tackling PIP as an increasing clinical and public health problem. While further study is required to determine how improved prescribing skills translate into everyday practice and their effect on patient outcomes, it is a logical and reasonable assumption that non-complex, e-learning interventions will benefit doctors and older patients alike.

4.5 Limitations

Participants in this trial were volunteers which presents an initial bias. There was a 45% drop-out rate from recruitment to the final assessment at 12 weeks. Both these factors potentially reduce the reliability of the findings. Drop-out data was not included in the analysis. One possible method of handling the missing data would be to employ the 'last observation carried forward (LOCF)' method. This involves simply imputing values for participants who have dropped out based on their last recorded results. However, in a recent advisory report, the National Academy of Sciences recommended against the use of methods like LOCF due to the risk of underestimating the treatment effect [226]. Finally, as mentioned above, this study did not explore if the intervention resulted in improved patient outcomes.

4.6 Conclusion

PIP is a widespread problem across multiple grades of doctors in multiple areas of practice. Doctors often lack confidence in their skills as prescribers for older patients and feel poorly equipped to manage the complexities associated with older people, particularly frailer older people with multi-morbidity and associated complex polypharmacy. A short e-learning module focused on geriatric pharmacotherapy can significantly improve doctors' prescribing skills and confidence with regards to older patients. Whether this results in actual improvements in appropriateness of prescribing for these patients remains to be seen.

5. Use of a frailty index to identify potentially inappropriate prescribing and adverse drug reaction risks in older patients

Chapter description

Chapters 2 and 3, clearly highlighted that doctors working lives, and working environments are chaotic and inconducive to appropriate prescribing. They simply do not have the time to review and assess every patients' chart for appropriateness. Chapter 3 also showed that interventions based on 'enablement' would be potentially beneficial in addressing PIP. Therfore, it was decided to explore the potential of an intervention based on highlighting patients at increased risk of PIP/ADRs to doctors by way of a simple indicator on the front of their chart or in their medical notes.

The work of this chapter has been accepted for publishing in Age and Ageing and is currently in press.

5.1 Introduction

Much quantitative research has taken place in recent times to identify the prevalence and severity of PIP. Interest is currently focused on identifying the causal factors surrounding this phenomenon in an effort to minimise and prevent PIP and its effects. Chapters 2, 3 and 4 identified several areas for such intervention [156, 215]. It has been shown that doctors often possess an inherent fear of changing a patient's prescription, even when they know it may not be appropriate for that patient [156]. For other prescribers, checking for appropriateness of medications is a low priority [156]. Doctors are quite aware that PIP is a significant problem, but busy working environments, lack of time for prescription surveillance and lack of specific geriatric pharmacotherapy training all serve as barriers to optimal prescribing for older patients in their minds [215]. Considering these issues, one can hypothesise that, if doctors were given a single indicator of PIP and consequent ADR risk on a patient's prescription, it might stimulate them to review the medicines on that prescription, with a view to minimising PIP. It was suggested that a frailty index (FI) score may be such a suitable indicator.

Frailty is defined as a clinical state in older vulnerable adults arising from age-associated decline in physiological functions across multiple organ systems, resulting in a diminished ability to respond to physiological stressors [227-230]. In recent years, the importance of frailty and its identification in older patients has been recognised and the literature has seen a rise in studies exploring the link between frailty and several adverse health outcomes related to cardiovascular health, cognitive performance, depression, quality of life, falls, post-op recovery,

altered pharmacokinetics of medications, hospitalisations and mortality [91, 231-238].

The pathogenesis of frailty has also been extensively researched and a number of key pathophysiological processes have been reported as instrumental in the development of frailty. Underlying chronic inflammation and immune system activation have been shown to be possibly the most significant contributory factor to frailty [239-254]. Loss of muscle mass and strength, also known as sarcopenia, has also been shown to be a likely contributor to frailty and research into same is regarded as a potential intervention area for frailty [255, 256]. Age-related declines in hormones such as oestrogen, testosterone, cortisol and vitamin D have also been linked to frailty [257-259], as well as mid-life obesity [260-263].

While frailty itself is a syndrome which requires therapy such as exercise and comprehensive geriatric assessments [227, 264-267], it is also considered a useful clinical tool for identification of adverse outcome risk in older patients [91, 229, 261, 268]. However, although there has been considerable efforts to reach international consensus on frailty [269], there has been much debate as to how best to define, measure and utilise frailty identification for this purpose. Several tools have been developed to identify and measure frailty such as FRAIL (Fatigue, Resistance, Ambulation, Illnesses, Loss of weight) (International Academy of Nutrition and Aging) [270], Frailty Instrument for Primary Care of the Survey of Health, Ageing and Retirement in Europe (SHARE-FI) [271], and the Groningen Frailty Indicator [272]. However two in particular have dominated the literature.

Firstly, the frailty phenotype, developed by Fried *et al.* diagnoses frailty if a patient meets three or more of five criteria:

(i) Weakness as measured by low grip strength

(ii) Slowness by slowed walking speed

(iii) Low level of physical activity

(iv) Low energy or self-reported exhaustion

(v) Unintentional weight loss [229].

The second, is the frailty index (FI) [273]. The FI is based on a comprehensive geriatric assessment by counting the number of deficits accumulated, including diseases, physical and cognitive impairments, psychosocial risk factors, and common geriatric syndromes. The number of variables included in an FI typically ranges from 30-70 [274] and each variable must meet 5 criteria to be included:

(i) The variables must be deficits associated with health status

(ii) A deficit's prevalence must generally increase with age

(iii) Similarly, the chosen deficits must not saturate too early

(iv) When considering the candidate deficits as a group, the deficits that make up an FI must cover a range of systems

(v) If a single FI is to be used on a sample of patients, the items that make up the FI need to be the same from one iteration to the next. The requirement to use the same items need not apply to comparisons between samples – i.e. samples that use difference FIs appear to yield

similar results [268, 275]. This is useful as the same information regarding deficits is not always available in different sites.

The number of deficits a patient has is then summated and the result is divided by the number of variables to yield an FI score of between 0 and 1.

The FI was originally developed as a means of assessing individual aging [276]. While age alone is an important determinant of health and survival, the older a population becomes, the more variance is observed in health [277] i.e individuals of the same age can differ greatly from each other in terms of general health, hence the need for a more accurate measurement of health status. Since the FI was developed, it has been extensively researched and assessed with regards to its relevance and generalizability [268, 278-282]. Interestingly, results from multiple different studies, all using different combinations of deficits have been consistent [275]. As reported by Searle et al: *"this indicates that frailty can be measured in many ways, and therefore can be studied in many existing datasets that might not have set out to measure frailty per se"* [275].

Recently, Cesari *et al.* showed that, although the frailty phenotype and frailty index are often thought of as alternatives to each other, they are different instruments, with different purposes, and should therefore be seen as complementary to one another [283].

There has been much debate as to how best to operationalise frailty assessment scales and utilise them effectively in everyday practise [284, 285]. The majority of studies exploring frailty and it's significance focus on the correlation between it and

mortality or adverse outcomes such as hospitalisation, self-reported quality of life, intensity of treatment, nursing home admission, after-hours GP visit or social vulnerability [286]. No published studies have explored the link between frailty and increased risk of potentially inappropriate prescribing (PIP) and adverse drug reactions (ADRs).

If a positive relationship between these entities exists, then an FI score above a certain threshold could be used as an indicator to prescribers that a patient's medications should be reviewed for instances of PIP/potential ADRs. Whether this approach is superior to, for example, just using the number of medications a patient takes to identify risk of PIP/ADRs is unknown.

The aim of this chapter is to determine whether such a relationship between a patient's frailty, the appropriateness of their medications and their likelihood of developing ADRs exists, and whether this is a more useful approach than just using the number of medications alone to identify patients for review.

5.2 Methods

An FI was constructed using methods outlined by Searle *et al.* [275], and applied to a database of comprehensive geriatric assessments for 737 hospital in-patients. Details of the construction of the FI are outlined below. An FI was chosen over a frailty phenotype as the frailty phenotype is typically more suitable when applied at first contact with the patient [283]. Also, the frailty phenotype may lose some of its clinical relevance when applied to older patients already experiencing disability [283], which it was felt would be the case in a high proportion of patients in the database.

The FI was then used to assign each patient an FI score. The correlation between this score and the number of instances of PIP on a patient's prescription, as well as patients' likelihood of developing ADRs was then explored and compared to just using the number of medications taken by the patient.

5.2.1 Construction of patient database

The database used for this study was previously compiled as part of a randomised controlled trial assessing the impact of a structured pharmacist intervention on the appropriateness of in-patients' medications [287]. In all, 737 patients underwent a comprehensive geriatric assessment on admission to hospital. Information relating to their physical and mental well-being was collected and these details were entered directly into an electronic database (Microsoft Access™).

5.2.2 Construction of frailty index

All the variables collected to form the database were assessed for suitability for inclusion in the FI using the criteria suggested by Searle *et al [275]*. Although it has been reported that frailty indices comprising a minimum of 50 variables are robust [283], shorter versions (as low as 20) have been utilised and shown to be sufficiently accurate for predicting adverse outcomes [278].

All binary variables were coded as 1 or 0 (1 indicating presence of the deficit, 0 indicating absence of the deficit). To code continuous variables, an interim index, consisting of only binary variables was established. The purpose of this interim index was to provide cut-off points for the continuous variables. These variables

were correlated with the interim index and the mean value corresponding to 0.2 on the interim index was used as that variable's cut-off point. An FI score of 0.2 is recognised by multiple frailty measures as approaching a frail state [229, 279, 280]. Using the completed index, each patient was then given an FI score by summating all the deficits present for that patient and dividing by the total number of variables.

5.2.3 Statistical analysis

To explore the relationship between frailty and appropriateness of patients' medications, each patient's FI score was correlated with the number of breaches of STOPP criteria (version 1) (Appendix XIV) [69] identified within that patient's prescription. Version 1 was used as this was the version originally applied to the database. STOPP criteria identify more common instances of PIP. The median number of breaches of the STOPP criteria was then determined for each point of the frailty score scale. Pearson correlation tests and linear regression using 95% confidence intervals were performed to quantify the relationship. The mean FI score above which patients were found to have at least one instance of PIP present on their prescription was then determined to identify an FI threshold that could be used to identify frailer older patients at risk of PIP/ADRs, and therefore needing medication review. A similar threshold was obtained for 'number of medications' so this could be compared to the FI to see which performed better in terms of identifying patients at risk of PIP/ADRs.

ADR ascertainment in the original RCT was based on the WHO ADR definiton, i.e. "*a response to a drug which is noxious and unintended and which occurs at doses*

normally used in man for the prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function". The research pharmacist performed ADR ascertainment, facilitated by the use of a pre-defined ADR trigger list consisting of the ten most common clinical manifestations of proven ADRs, derived from a combined database of two recent studies of 600 [24] and 513 [38] elderly hospitalized patients. For each ADR, the primary researcher recorded details of the suspect medication(s), i.e. dose, formulation and duration, as well as a description of the ADR and any actions taken to resolve it. A physician trained in Geriatric Medicine and experienced in Geriatric Pharmacology/Therapeutics reviewed and verified all ADRs identified by the primary researcher.

The number of patients experiencing at least one instance of PIP/ADR within 7 days of their hospital stay, on both sides of this threshold was then compared. The extent to which an instance of PIP/ADR was dependent on frailty was quantified by a chi-square test, and the risk associated with being in either group was determined by calculating odds ratios.

This same procedure was applied using the 'number of medications' threshold.

Ethical approval for this study was sought from and granted by the Clinical Research Ethics Committee, University College Cork (Appendix XV).

5.3 Results

From all the variables in the database, 34 were deemed suitable for inclusion in the FI as per the methods proposed by Searle *et al* [275]. 711 patients in the database had the information required for inclusion. Mean age of participants was 74. Of the

34 variables, 32 were binary and 2 were continuous (number of medications and abbreviated mental test score (AMTS)). The variables and their cut off points (for the continuous variables) are displayed in **Table 5.1**. These were determined by correlating the continuous variables with the interim index consisting only of binary variables, and identifying the values corresponding to a frailty score of 0.2 on the interim index.

Table 5.1: Variables and cut-off points used for frailty index

	Variable	**Cut-off point**
1.	Needs help grooming	Yes=1 No=0
2.	Needs help using toilet	Yes=1 No=0
3.	Needs help feeding	Yes=1 No=0
4.	Needs help with transfer	Yes=1 No=0
5.	Needs help mobilising	Yes=1 No=0
6.	Needs help dressing	Yes=1 No=0
7.	Needs help with stairs	Yes=1 No=0
8.	Needs help bathing	Yes=1 No=0
9.	Dementia/cognitive impairment	Yes=1 No=0
10.	On-going constipation	Yes=1 No=0
11.	Fall in the last 3 months	Yes=1 No=0
12.	Difficulty swallowing	Yes=1 No=0
13.	Trouble sleeping	Yes=1 No=0
14.	Previous myocardial infarction	Yes=1 No=0

15.	Hypertension	Yes=1 No=0
16.	Congestive cardiac failure	Yes=1 No=0
17.	Peripheral vascular disease	Yes=1 No=0
18.	Cerebrovascular disease	Yes=1 No=0
19.	Chronic pulmonary disease	Yes=1 No=0
20.	Rheumatological disease	Yes=1 No=0
21.	Peptic ulcer disease	Yes=1 No=0
22.	Mild or moderate liver disease	Yes=1 No=0
23.	Diabetes	Yes=1 No=0
24.	Diabetes with complications	Yes=1 No=0
25.	Hemiplegia or paraplegia	Yes=1 No=0
26.	Renal disease	Yes=1 No=0
27.	Any malignancy	Yes=1 No=0
28.	Moderate or severe liver disease	Yes=1 No=0
29.	Metastatic solid tumour	Yes=1 No=0
30.	Incontinence (bowels)	Yes=1 No=0
31.	Incontinence (bladder)	Yes=1 No=0
32.	Self-reported depression	Yes=1 No=0
33.	Number of medications	>=6=1 <6=0
34.	AMTS (Abbreviated Mental Test Score)	<=8=1 >8=0

FI scores among the 711 patients ranged from 0 to 0.51, with a mean of 0.15 (±0.09). Data was normally distributed with a slight positive skew (skewness = 1.137), see **Figure 5.1**.

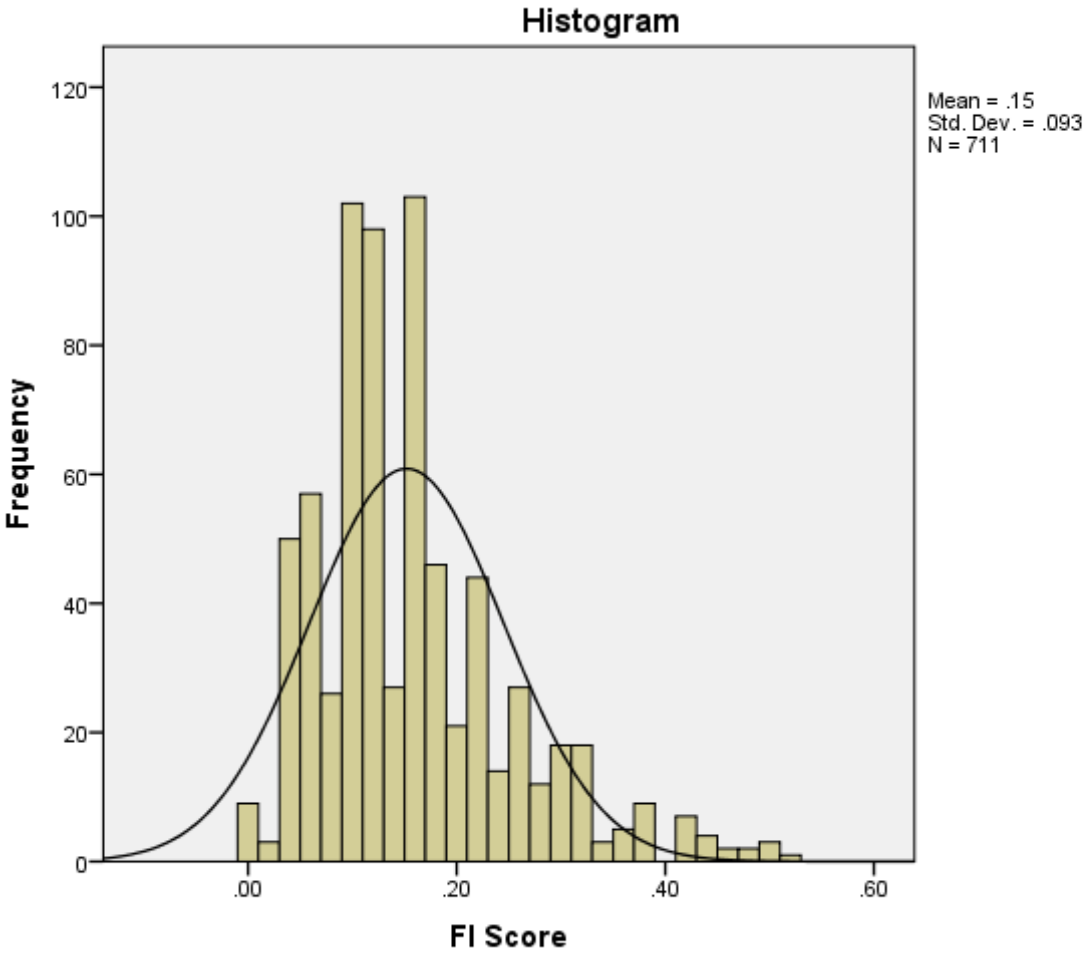


Figure 5.1: Distribution of Frailty Index (FI) scores

403 patients experienced at least one instance of PIP, defined by a breach of the STOPP guidelines, within seven days of their hospital stay. In these 403 patients, there were a total of 733 instances of PIP.

Figure 5.2 shows the frailty scores plotted against the median number of breaches of the STOPP criteria for each observed point on the FI scale. A significant correlation between FI score and median number of STOPP breaches was observed (R=0.92). Median was chosen as although the number of breaches of the STOPP criteria was also normally distributed, the skewness was greater (skewness = 2.011).

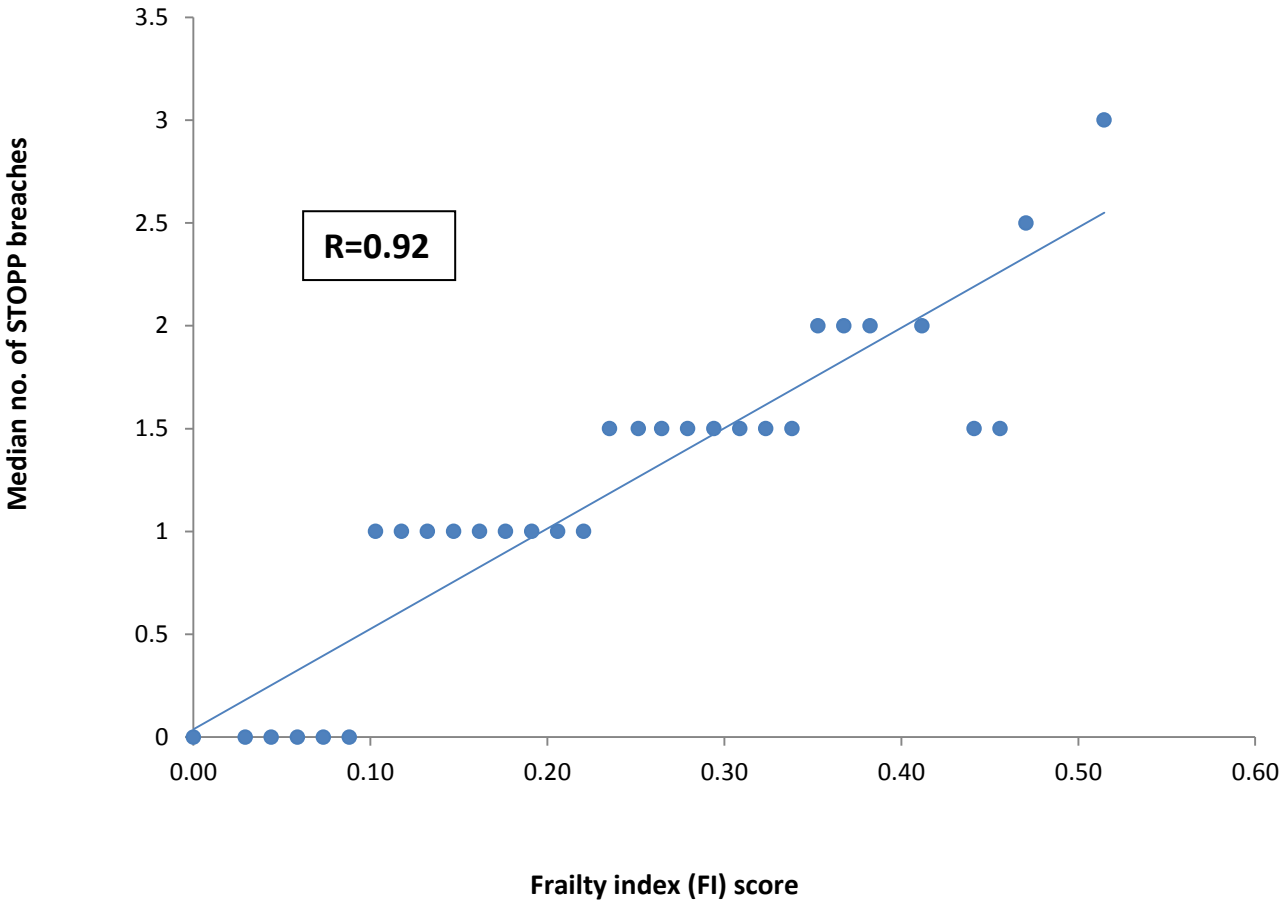


Figure 5.2: Frailty index score plotted against Median number of breaches of the STOPP criteria

Table 5.2 summarises the results of the Pearson correlation and linear regression tests. The Pearson coefficient of 0.92 is significant ($p < 0.0001$). The R squared value of 0.837 illustrates that 83.7% of the variance within the number of instances of PIP experienced by patients can be accounted for by their FI scores. The

unstandardized beta coefficient of 0.488 suggests that for each 0.1 rise in FI score, the number of instances of PIP rises by 0.488. The intercept value of 0.04 is the number of instances of PIP that can be expected when FI score is equalled to zero.

Table 5.2: Results of Pearson correlation and linear regression

	Value	**P value**	**95% confidence intervals**
Pearson correlation (R)	0.915	< 0.0001	N/A
R squared	0.837	N/A	N/A
Unstandardised Beta coefficient	0.488	N/A	0.4062 , 0.5698
Intercept	0.04	N/A	-0.187 , 0.267

To determine the threshold above which a patient should be brought to the attention of the prescriber, the mean FI score at which the median number of STOPP breaches was equal to one i.e the FI score at which patients had at least one instance of PIP on their prescription was calculated. This was shown to be 0.16. **Figure 5.3** shows how this threshold was determined.

As the 'number of medications' is a continuous variable in the FI the threshold for this was determined as described above, by identifying the mean number of medications taken by patients with a FI score of 0.2 on the interim index. This was found to be 6.

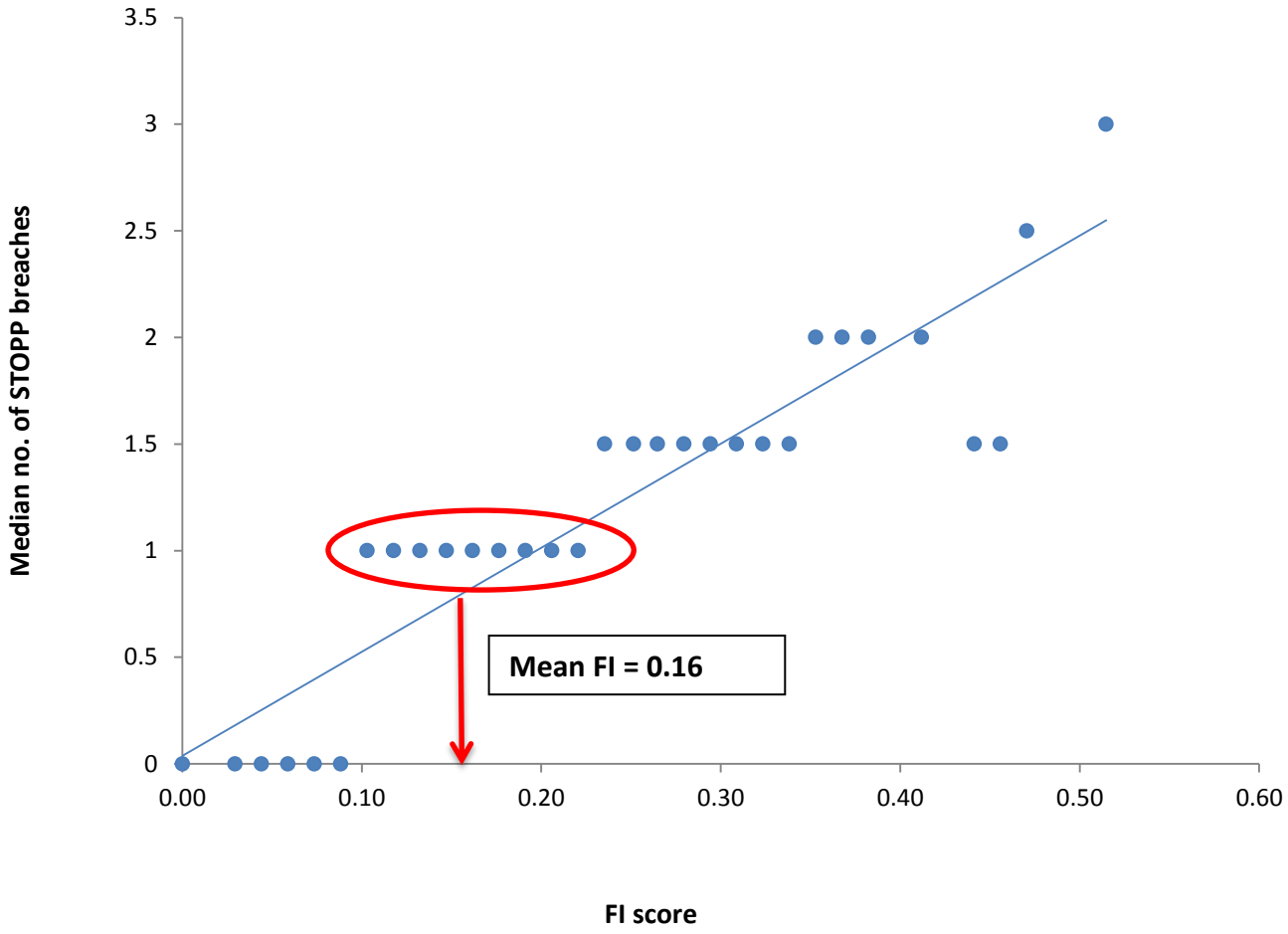


Figure 5.3: The mean FI score, above which patients had at least one instance of PIP present on their prescription is 0.16

In order to determine if adverse outcomes such as PIP and ADRs are actually dependent on frailty status/number of medications, chi square tests were performed using the following cross-tabulations, **Tables 5.3 and 5.4.** The results are summarised in **Table 5.5**.

Table 5.3: The differences in PIP/ADR occurrence on both sides of frailty index threshold (expressed as number of patients experiencing/not experiencing at least 1 instance of PIP/ADR)

	Patients with PIP	**Patients with No PIP**	**Total**
Frailty index score < 0.16	155	192	347
Frailty index score ≥ to 0.16	248	116	364
Total	**403**	**308**	**711**
	Patients with ADRs	**Patients with No ADRs**	**Total**
Frailty index score < 0.16	57	290	347
Frailty index ≥ to 0.16	107	257	364
Total	**164**	**547**	**711**

Table 5.3 shows the number of patients that experienced at least 1 instance of PIP, as well as the number of patients who experienced no PIP, both above and below the FI threshold of 0.16. 68.1% of patients with an FI score of greater than or equal to 0.16 experienced at least one instance of PIP compared to just 44.7% of patients with score of less than 0.16. Also displayed in **Table 5.3** is the number of patients that experienced at least 1 ADR, as well as the number of patients who experienced no ADRs, both above and below the FI threshold. 29.4% of patients with an FI score greater than or equal to 0.16 experienced at least on ADR compared to just 16.4% of patients with score of less than 0.16.

Table 5.4: The differences in PIP/ADR occurrence on both sides of the number of medications threshold (expressed as number of patients experiencing/not experiencing at least 1 instance of PIP/ADR)

	Patients with PIP	**Patients with No PIP**	**Total**
< 6 medicines	77	128	205
≥ 6 medicines	326	180	506
Total	**403**	**308**	**711**
	Patients with ADRs	**Patients with No ADRs**	**Total**
< 6 medicines	55	150	205
≥ 6 medicines	109	397	506
Total	**164**	**547**	**711**

Table 5.4 shows number of patients that experienced at least 1 instance of PIP, as well as the number of patients who experienced no PIP, both above and below the 'number of medications' threshold of 6. 64.4% of patients taking 6 or more medications experienced at least one instance of PIP compared to just 37.6% of patients with less than 6 medications.

Also displayed in **Table 5.4** is the number of patients that experienced at least 1 ADR, as well as the number of patients who experienced no ADRs, both above and below the 'number of medications' threshold. 21.5% of patients with 6 or more medications experienced at least one ADR compared to just 26.8% of patients with less than 6 medications.

Table 5.5 compares the FI with just using 'number of medications' by way of association with PIP and ADR occurrence.

Table 5.5: Association between frailty index score, number of medication, PIP occurrence and ADR occurrence

Patients with FI score ≥ to 0.16	**% Experiencing at least 1 ADR**	**Odds ratio and 95% CI**	**Chi-square**	***p* value**
	29.4% (Compared to 16.7% of patients with FI < 0.16)	2.1 (1.474, 3.044)	16.030	<0.0001
	% Experiencing at least 1 instance of PIP	**Odds ratio and 95% CIC**	**Chi-square**	***p* value**
	68.1% (Compared to 44.7% of patients with FI < 0.16)	2.6 (2.0, 3.6)	39.831	<0.0001
Patients taking more than 6 medications	**% Experiencing at least 1 ADR**	**Odds ratio and 95% CI**	**Chi-square**	***p* Value**
	21.5% (Compared to 26.8% of patients with less than 6 medicines)	0.75 (0.515 , 1.089)	2.299	0.129
	% Experiencing at least 1 instance of PIP	**Odds ratio and 95% CIC**	**Chi-square**	***p* value**
	64.4% (Compared to 37.6% of patients with less than 6 medicines)	3.01 (2.15 , 4.21)	42.887	<0.0001

Patients with an FI score greater than or equal to 0.16 were twice as likely to experience at least one instance of PIP, and twice as likely to experience at least one ADR during the index hospitalisation.

Instances of PIP and instances of ADRs were found to be significantly dependent on frailty scores ($p < 0.0001$ for both.)

Patients taking more than 6 medications were not statistically more likely to experience an ADR, however, were 3 times more likely to experience at least one instance of PIP.

PIP was found to be highly dependent on number of medications taken ($p<0.0001$). ADR occurrence was not significantly dependent on number of medications ($P=0.129$)

5.4 Discussion

5.4.1 Implications for clinical practice

The principal novel findings in this study are:

(i) A significant positive relationship between a patient's frailty status and the appropriateness of their medications exists. This is a clinically relevant finding as frailty is relatively easily quantified using an FI, when compared to medication appropriateness, which is not as easily determined, and is often not acted upon when PIP is identified [156]. These findings show that an FI score greater than 0.16 would be a suitable prompt for prescribers to review a patient's medications, with a view to minimising PIP.

(ii) As mentioned, an FI score of 0.2 has traditionally been accepted as 'approaching frailty' [229, 279, 280]. It appears logical therefore to use this as the threshold, above which a patient's prescription would be highlighted to a prescriber for review. However, the present study shows that at a frailty score of 0.16 and above, most patients will have at least one instance of PIP on their prescription list. This difference of 0.04 in the FI score equates to 1 less deficit a patient would need to be

considered ‘at risk’ (using a 34 variable FI such as the one presented here). This becomes significant when we consider that 95% of the patients in the database had less than 10 of the deficits in the frailty index.

(iii) The results of the statistical analysis strengthen the argument for using an FI score as a means of identifying patients at risk of PIP and associated ADRs. Almost 84% of the variance within the number of instances of PIP was accounted for by patients’ FI scores. Highly significant *p* values and odds ratios greater than 2.0, all indicate that patients with an FI score ≥ 0.16 are at significantly increased risk of PIP and ADRs. Furthermore, when the FI is compared to just using ‘number of medications’, we see that while both ADR and PIP occurrence are significantly dependent on FI scores, only PIP is significantly dependent on ‘number of medications’. In fact, patients taking more than 6 medications were 3 times more likely to experience PIP. Therefore, while this suggests an FI is superior in terms of identifying patients at risk of *both* ADRs and PIP, utilisation of *both* a frailty index threshold *and* a ‘number of medications’ threshold would seem to be the optimum i.e patients with FI score ≥ 0.16 and taking more than 6 medications are at high risk for PIP and ADRs.

FI scores and PIP criteria may not secure the attention of some prescribers. However, most physicians are aware of ADRs and accept that they are an area of concern in frailer older patients [288]. Therefore, if a patient is highlighted to a doctor on the basis of a frailty score above a threshold that indicates a heightened risk of that patient experiencing an ADR, it is likely to carry more significance to the

doctor than simply indicating that the patient is taking a potentially inappropriate medication (PIM).

5.4.2 Implications for future research

Implementation of this initiative to determine if it successfully reduces PIP rates and ADR rates in a clinical setting is the next logical step in terms of research. This idea of intervention based on the concept of enablement has recently been suggested as an area that should be targeted to reduce PIP [215]. Historically, the quality of interventions aimed at reducing PIP has been questionable [289]. However, it is only in recent times that qualitative research methodologies have been utilised to inform such interventions. If these methodologies are implemented correctly, the result could be more targeted interventions with quantifiably better clinical outcomes.

It should also be considered, that while older patients are often under the care of multiple doctors, their primary care physician is in the best position to oversee the management of their care. Previous studies have shown that a FI can be operationalised in primary care using routinely gathered data [290, 291]. Future research in primary care settings, identifying cut-off points for continuous variables and implementing systems to identify frailty could potentially lead to improved care for these patients.

While it has been shown that an intervention based upon highlighting patients with an FI score above a certain threshold to prescribers for careful medication review would be justified, nevertheless, educational interventions focused on specific aspects of geriatric pharmacotherapy are still required to enable doctors make

clinically sound decisions in frailer, older, multi-morbid patients with polypharmacy. This need for tailored training has been raised in several studies to date and has also been shown to be effective in preventing PIP [52, 215].

5.5 Limitations

The dataset used for this study was limited to 711 patients.

A prospective study to validate the FI would be of benefit.

The health economic impact of the tool and its implications would be warranted.

While much of the patient data used to create the FI is routinely available, collecting all the data required may be somewhat complex in secondary care and may negatively impact the feasibility of such an initiative being implemented.

The dataset used for this study utilised STOPP/START version 1. The STOPP/START guidelines have since been updated and now contain 22 new STOPP rules and 12 new START rules as well as new categories in each [70] (Appendix XIII). Given that this study used breaches of STOPP/START criteria to determine appropriateness of patients' medications, the methodologies should be repeated using the updated guidelines.

The max FI score in this study was 0.51. This is considerably lower than the commonly reported 99% limit to deficit accumulation seen in secondary care (0.69) [292]. This limits the generalisability of these results and warrants further research.

5.6 Conclusion

A significant positive relationship exists between a patient's frailty status, the appropriateness of their medications and their likelihood of developing an ADR. At an FI score of 0.16 and higher, patients are twice as likely to have at least one PIM prescribed. Also, patients above this threshold are twice as likely to experience an ADR compared to those below the threshold. While ADR occurrence is not significantly dependent on the number of medications a patient takes, PIP is. Therefore the use of both a FI as well as 'number of medications' seems the best approach to identify patients at risk.

6. Application of a frailty index threshold to identify older patients at risk of potentially inappropriate prescribing and adverse drug reactions: A prospective observational study

Chapter description

In this chapter, the findings from chapter 5 were applied to a different patient group using a modified version of the frailty index to validate and reinforce the conclusions in the previous chapter.

6.1 Introduction

In chapter 5, it was shown that there is significant correlation between a patient's frailty status (as measured by the frailty index (FI)), and their propensity to experience PIP and ADRs (R=0.92). It was found that at an FI score of 0.16 and above, patients were twice as likely to experience both PIP and ADRs ($p<0.0001$). This approach was compared to using the number of medications a patient took as an indicator of PIP/ADR risk. This revealed that while the FI threshold of 0.16 identified patients at risk of *both* PIP and ADRs, just using a 'number of medications' threshold of 6 (identified by correlating number of medications to an interim FI), was only useful in identifying patients at risk of PIP, albeit PIP was found to be *highly* dependent on the number of medications. Patients above this threshold were three times more likely to experience PIP ($p<0.0001$). It was concluded therefore, that using *both* an FI and number of medications as tools to identify patients at risk of PIP/ADRs was superior to using either method in isolation i.e patients with an FI score ≥ 0.16 *and* taking 6 or more medications are at high risk of PIP/ADRs.

The aims of this chapter were:

(i) To apply the FI threshold of 0.16 to a new set of patients' data to determine if the results seen in Chapter 5 are reproducible, and in doing this, validate those results,

(ii) To compare the use of an FI in isolation to using the number of medications a patient takes to identify those at risk of PIP/ADRs.

6.2 Methods

An FI was constructed using methods outlined by Searle *et al.* [275], and applied to comprehensive geriatric assessments for 545 hospital in-patients. Details of the construction of the FI are outlined below.

The FI was then used to assign each patient an FI score. Patients above and below the threshold of 0.16 were identified and the relationship between their frailty status and instances of PIP (as defined by the STOPP guidelines [69]) and ADRs was then explored to determine if this threshold identifies patients at risk. This was compared to simply using the number of medications threshold of 6, as in Chapter 5.

6.2.1 Patient group

This study was carried out as a sub-study of an ongoing, larger randomised controlled trial (Development and clinical trials of a new Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons-SENATOR) in six hospitals across Europe. The sites include:

(i) Cork University Hospital, Ireland

(ii) Ghent University Hospital, Belgium

(iii) Hospital Universitario Ramón y Cajal, Spain

(iv) Landspitali University Hospital Reykjavik, Iceland

(v) Aberdeen Royal Infirmary, Scotland

(vi) Ospidale Riuniti, Ancona, Italy.

As per the SENATOR trial protocol, patients over the age of 65 presenting to the emergency department with an acute illness requiring admission, ≥ 3 chronic medical disorders and being under the care of a specialist other than a geriatrician, palliative medicine physician, haematologist, oncologist or clinical pharmacologist were included in the study within 72 hours of arrival. Exclusion criteria included: elective hospitalisation, direct admission to intensive care unit and documented plan for consultation with geriatric medicine. All patients signed a consent form after they were informed of the study. In the case of cognitive impairment, a care-giver signed consent by proxy.

6.2.2 Construction of the frailty index

All the variables collected as part of the SENATOR trial were assessed for suitability for inclusion in the frailty index using the criteria suggested by Searle et al [275].

All binary variables were coded as 1 or 0 (1 indicating presence of the deficit, 0 indicating absence of the deficit). To code continuous variables, an interim index, consisting of only binary variables was established. The purpose of this interim index was to provide cut-off points for the continuous variables. These variables were correlated with the interim index and the mean value corresponding to 0.2 on the interim index was used as that variable's cut-off point. An FI score of 0.2 is recognised by multiple frailty measures as approaching a frail state [229, 279, 280]. Using the completed index, each patient was then given an FI score by summating all the deficits present for that patient and dividing by the total number of variables.

6.2.3 Statistical analysis

The numbers of patients experiencing at least one instance of PIP/ADR within 7 days of their hospital stay, on both sides of the FI threshold were then compared. The extent to which an instance of PIP/ADR was dependent on frailty was quantified by a chi-square test, and the risk associated with being in either group was determined by calculating odds ratios.

This same procedure was applied using the 'number of medications' threshold.

Ethical approval for this study was sought from and granted by the Clinical Research Ethics Committee, University College Cork as part of the SENATOR study (see appendix XVI).

6.3 Results

From all the deficits measured as part of the SENATOR trial, 34 were deemed suitable for inclusion in the FI as per the methods proposed by Searle *et al.* [275]. Twenty of these were identical to those used in chapter 5. The full list of 34 variables is presented in **Table 6.1**. While not identical to those in Chapter 5, these variables still cover the same array of physiological systems and deficits. 518 patients had the information required for inclusion as of July 2015. Mean age of participants was 82 (±7 years). Of the 34 variables, 32 were binary and 2 were continuous (number of medications and Mini Mental State Examination (MMSE) score). The variables and their cut off points (for the continuous variables) are displayed in **Table 6.1**. These were determined by correlating the continuous

variables with the interim index consisting only of binary variables, and identifying the values corresponding to a frailty score of 0.2 on the interim index.

Table 6.1: Variables and cut-off points used for frailty index. Variables marked with * did not appear in Chapter 5

	Variable	**Cut-off point**
1.	Needs help grooming	Yes=1 No=0
2.	Needs help using toilet	Yes=1 No=0
3.	Needs help feeding	Yes=1 No=0
4.	Needs help with transfer	Yes=1 No=0
5.	Needs help mobilising	Yes=1 No=0
6.	Needs help dressing	Yes=1 No=0
7.	Needs help with stairs	Yes=1 No=0
8.	Needs help bathing	Yes=1 No=0
9.	Dementia/cognitive impairment	Yes=1 No=0
10.	Respiratory disease (other than COPD)*	Yes=1 No=0
11.	Fall in the last 3 months	Yes=1 No=0
12.	Upper GI disease*	Yes=1 No=0
13.	Lower GI disease*	Yes=1 No=0
14.	Chronic Pain/discomfort*	Yes=1 No=0
15.	Hypertension	Yes=1 No=0
16.	Congestive cardiac failure	Yes=1 No=0
17.	Previous ADR*	Yes=1 No=0
18.	Cerebrovascular disease	Yes=1 No=0

19.	Delirium*	Yes=1 No=0
20.	Arthritis*	Yes=1 No=0
21.	COPD*	Yes=1 No=0
22.	Mild or moderate liver disease	Yes=1 No=0
23.	Diabetes	Yes=1 No=0
24.	Vision impairment*	Yes=1 No=0
25.	Hearing impairment*	Yes=1 No=0
26.	Renal disease	Yes=1 No=0
27.	Stroke*	Yes=1 No=0
28.	Osteoporosis*	Yes=1 No=0
29.	Malnutrition*	Yes=1 No=0
30.	Incontinence (bowels)	Yes=1 No=0
31.	Incontinence (bladder)	Yes=1 No=0
32.	Self-reported depression	Yes=1 No=0
33.	Number of medications	≥ 6=1 < 6=0
34.	Mini Mental State Examination (MMSE)*	≤ 25=1 >25=0

FI scores among the 518 patients ranged from 0.06 to 0.85, with a mean of 0.36 (±0.16). Data was normally distributed with a slight positive skewness (skewness = 0.419), see **Figure 6.1**.

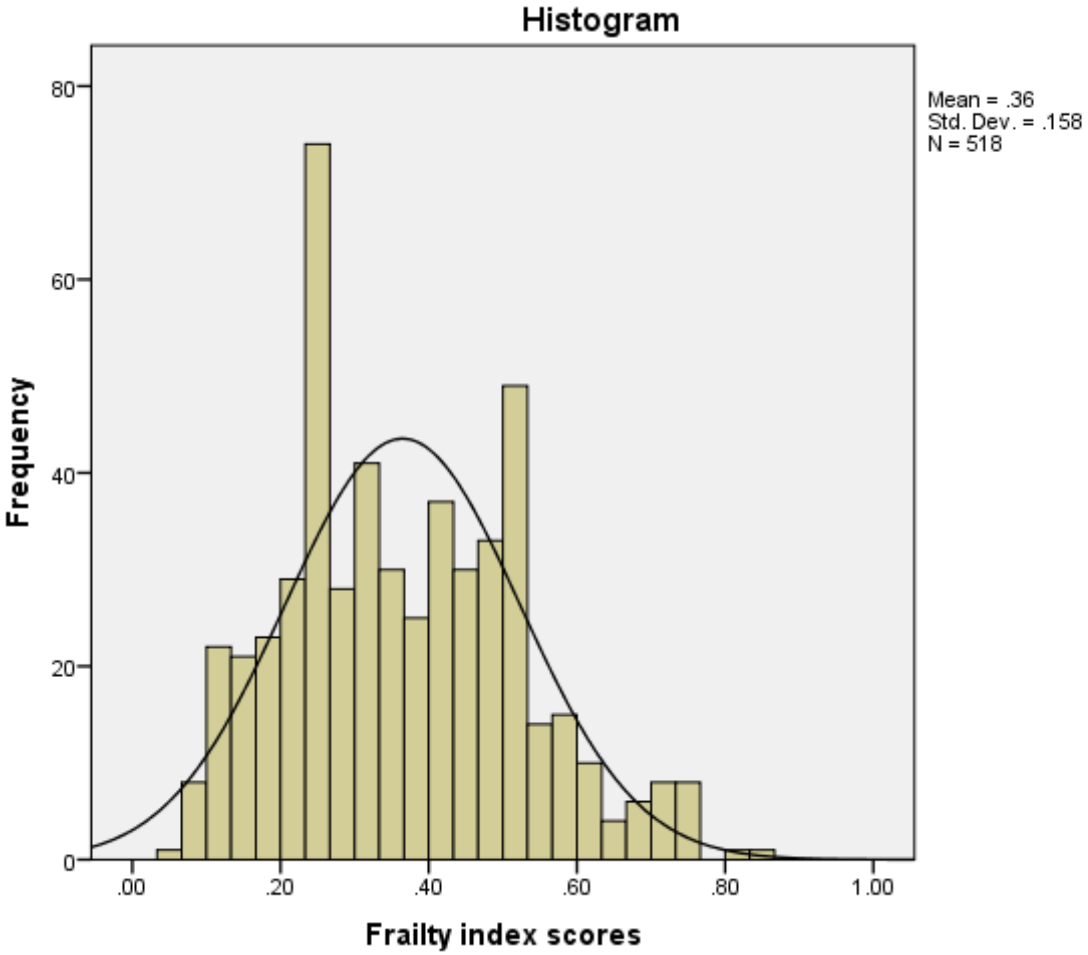


Figure 6.1: Distribution of frailty index scores

351 patients experienced at least one instance of PIP, defined by a breach of the STOPP guidelines, within seven days of their hospital stay. 253 patients experienced at least 1 ADR.

In order to determine if adverse outcomes such as PIP and ADRs are actually dependent on frailty status/number of medications, chi square tests were

performed using the following cross-tabulations, **Tables 6.2 and 6.3**. The results are summarised in **Table 6.4**.

Table 6.2: The differences in PIP/ADR occurrence on both sides of frailty index threshold (expressed as number of patients experiencing/not experiencing at least 1 instance of PIP)

	Patients with PIP	**Patients with No PIP**	**Total**
Frailty index score < 0.16	31	21	52
Frailty index score ≥ to 0.16	320	146	466
Total	351	167	**518**
	Patients with ADRs	**Patients with No ADRs**	**Total**
Frailty index score < 0.16	14	38	52
Frailty index score ≥ to 0.16	239	227	466
Total	253	265	**518**

Table 6.2 shows the number of patients that experienced at least 1 instance of PIP, as well as the number of patients who experienced no PIP, both above and below the FI threshold of 0.16. 68.7% of patients with an FI score of greater than or equal to 0.16 experienced at least one instance of PIP compared to 59.6% of patients with score of less than 0.16. Also displayed in **Table 6.2** is the number of patients that experienced at least 1 ADR, as well as the number of patients who experienced no ADRs, both above and below the FI threshold of 0.16. 51.3% of patients with an FI score greater than or equal to 0.16 experienced at least on ADR compared to just 26.9% of patients with score of less than 0.16.

Table 6.3: The differences in PIP/ADR occurrence on both sides of the number of medications threshold (expressed as number of patients experiencing/not experiencing at least 1 instance of PIP)

	Patients with PIP	**Patients with No PIP**	**Total**
Number of meds < 6	108	87	195
Number of meds ≥ to 6	243	80	323
Total	351	167	**518**
	Patients with ADRs	**Patients with No ADRs**	**Total**
Number of meds < 6	88	107	195
Number of meds ≥ to 6	165	158	323
Total	253	265	**518**

Table 6.3 shows number of patients that experienced at least 1 instance of PIP, as well as the number of patients who experienced no PIP, both above and below the 'number of medications' threshold of 6. 75.2% of patients taking 6 or more medications experienced at least one instance of PIP compared to 55.4% of patients with less than 6 medications.

Also displayed in **Table 6.3** is the number of patients that experienced at least 1 ADR, as well as the number of patients who experienced no ADRs, both above and below the 'number of medications' threshold. 51.1% of patients with 6 or more medications experienced at least one ADR compared to 45.1% of patients with less than 6 medications.

Table 6.4 compares the FI with just using 'number of medications' by way of association with PIP and ADR occurrence.

Table 6.4: Association between frailty index score, number of medications, PIP occurrence and ADR occurrence

Patients with FI score ≥ to 0.16	**% Experiencing at least 1 ADR**	**Odds ratio and 95% CI**	**Chi-square**	***p* value**
	51.3% (Compared to 26.9% of patients with FI < 0.16)	2.86 (1.51, 5.42)	11.114	0.001
	% Experiencing at least 1 instance of PIP	**Odds ratio and 95% CIC**	**Chi-square**	***p* value**
	68.7% (Compared to 59.6% of patients with FI < 0.16)	1.49 (0.83, 2.67)	1.755	0.185
Patients taking more than 6 medications	**% Experiencing at least 1 ADR**	**Odds ratio and 95% CI**	**Chi-square**	***p* Value**
	51.1% (Compared to 45.1% of patients with less than 6 medications)	1.27 (0.89 , 1.81)	1.726	0.189
	% Experiencing at least 1 instance of PIP	**Odds ratio and 95% CIC**	**Chi-square**	***p* value**
	75.2% (Compared to 55.4% of patients with less than 6 medications)	2.45 (1.68 , 3.57)	21. 926	<0.0001

Patients with an FI score greater than or equal to 0.16 were 2.86 times more likely to experience at least one ADR, and 1.49 times more likely to experience at least one instance of PIP within 7 days of admission compared to patients with FI scores less than 0.16.

Instances of ADRs were found to be significantly dependent on frailty scores ($p = 0.001$). However, were instances of PIP were not significantly dependent on frailty ($p = 0.185$).

Patients taking more than 6 medications were 1.27 times more likely to experience an ADR, and 2.45 times more likely to experience at least one instance of PIP.

In direct contrast to the FI results, PIP was found to be highly dependent on number of medications taken ($p<0.0001$), whereas ADR occurrence was not significantly dependent on number of medications ($p=0.189$)

6.4 Discussion

The findings of this study reflect the findings in Chapter 5 while also uncovering some differences. In Chapter 5, *both* ADRs and PIP were found to be significantly dependent on patients' frailty status (whether they were above or below the threshold of 0.16) with odds ratios greater than 2 and $p<0.0001$ for both. This study however has shown *just* ADRs to be significantly dependent on frailty status (ADRs: OR = 2.86, $p = 0.001$ Vs PIP: OR = 1.49, $p = 0.185$). In Chapter 5, PIP was found to be highly dependent on the number of medications a patient took (whether they were above or below the threshold of 6) with an odds ratio of 3.01 and $p<0.0001$. ADRs were not significantly dependent on the number of medications a patient took (OR = 0.75, $p = 0.129$). This study has reproduced this finding. Patients taking 6 or more medications were twice as likely to experience PIP ($p<0.0001$) but ADRs were not significantly dependent on the number of medications taken (OR = 1.27, $p = 0.189$).

So although there were some minor differences between the studies, namely the significance of the relationship between frailty status and PIP, the overall message from Chapter 5 remains true here i.e use of an FI threshold of 0.16 successfully identifies patients at risk of ADRs, and use of a 'number of medications' threshold of 6 successfully identifies patients at risk of PIP. Therefore, utilisation of *both* methods of detection is the optimum for identifying patients at risk of PIP/ADRs.

The FIs used in Chapter 5 and in the present study differed in terms of the variables used. This study utilised data collected from 5 different hospitals in 5 different countries. Therefore all the identical deficit information used in Chapter 5 was not available in each site. It has previously been reported that FIs using different variables yield similar results when comparing different patient groups [275]. The range of FI scores and the mean FI score in this study differ from Chapter 5, and are more in-line with reported FI scores, in secondary care [292]. This might appear to conflict with the above statement. However, the overall findings remained constant across the studies, suggesting that FIs which are customised to include deficit information available in specific sites can be compared effectively. The higher mean FI score and higher max value in this study may be explained by the higher mean age of 82 compared to 74 in chapter 5. This was simply an older, frailer population. Therefore, the differences in reported FI scores are not necessarily a reflection of inconsistencies between the FIs, but rather are a reflection of the differences in patient populations.

6.5 Limitations

This study was limited to 518 patients. Larger studies would be beneficial to further validate the results.

For sites with electronic prescribing and electronic medical records the collation of data for the FI would be relatively swift. However, where this is not the case, as in the Republic of Ireland, data collection may be somewhat laborious. Also, while much of the data included in the FI is routinely gathered information on admission which is readily available, some of it is not so accessible and may be limited to the researchers capabilities and amount of time available for data collection eg malnutrition, MMSE, previous ADRs.

6.6 Conclusion

The findings from Chapter 5 and this study suggest that using an FI threshold, as well as the number of medications a patient takes, as indicators to identify patients at risk of PIP and ADRs could potentially be a beneficial initiative to aid physicians in optimising prescribing for older patients. Time restraints, chaotic working environments and lack of training in geriatric medicine have all been suggested by prescribers as barriers to prescription reviews [156, 215]. Therefore a simple indication on the patient's case notes, such as a ticked box to indicate a patient above the thresholds, would seem a logical and useful activity. Whether this results in reduced instances of PIP and ADRs in routine clinical practice requires further research.

7. Could the Structured HIstory taking of Medication use (SHiM) tool optimise prescribing for older patients and reduce adverse events?

Chapter description

In an effort to identify more ways to optimise prescribing in older patients, and again, target 'enablement' as an intervention type, the SHiM tool was assessed on its potential ability to prevent adverse events in older patients.

The work of this chapter is currently under review for publication in the International Journal of Clinical Pharmacy

7.1 Introduction

It has been shown that on admission to hospital, almost 60% of older patients' medication lists contain at least one discrepancy compared to what they actually take at home [102, 293-295]. Discrepancy rates as high as 83% have been reported [296]. Medication history errors can result in adverse drug events (ADEs), patient harm and increased costs [296, 297]. In the studies carried out to date, 22-59% of medication history errors have had potential to cause harm based on propensity for harm criteria [296, 298-300]. Older patients, due to polypharmacy, co-morbidities and frequent exposure to multiple prescribing doctors are particularly susceptible to medication history errors [301, 302].

Medication reconciliation at the point of admission to hospital can reduce medication discrepancies and ADEs [303-306]. A number of definitions for medication reconciliation have been proposed in the past [307-310]. Essentially, medication reconciliation is the process of comparing a patient's medication list at the point of assessment, with what the patient actually takes at home, while noting any discrepancies and changes [311]. In 2007, the World Health Organisation expanded this definition by suggesting that medication reconciliation should also include a review of the *appropriateness* of patients' medications [312].

Until recently, there had been no structured format to the medication reconciliation process. Multiple sources had typically been used to determine patients' medication lists, such as community pharmacy records, general practitioner records, patients' own medication lists as well as their actual medicines brought into hospital. None of these sources on their own has been shown to be

completely accurate [313] and none has been used in a structured fashion [303, 314, 315].

In 2011, Drenth-van Maanen *et al.* developed a questionnaire, the **S**tructured **HI**story taking of **M**edication use (**SHiM**), to provide a structure for taking a detailed medication history in older people [300]. SHiM is based on multiple sources [309, 316] and consists of 21 questions exploring patients' current and recent medication use, practical problems concerning their medications, medication knowledge, beliefs about medicine and drug allergies/intolerances.

In a prospective study in which SHiM was applied to 100 older patients on admission to hospital in Utrecht, Netherlands, and compared to standard care, Drenth-van Maanen *et al.* found that SHiM revealed discrepancies with the medication lists obtained by the physician in 92% of patients [300]. Seventy-two percent of these discrepancies were judged to be potentially clinically relevant, while retrospective analysis of actual clinical events revealed that 21% of patients experienced actual clinical consequences arising from medication history discrepancies [300]. This study was, however, small scale - it only comprised 100 patients. Beyond this initial study, there has been very little research with regards to SHiM and its application to older patients. In addition, there was potential over-estimation of results in the above study due to recall bias [300]. Therefore, we cannot be certain as to the true impact of SHiM on older patients' prescriptions.

The aim of this chapter was to determine whether application of SHiM could optimise older patients' prescriptions on admission to hospital, and in-turn reduce ADEs, compared to standard care.

7.2 Methods

7.2.1 Setting and study population

A prospective observational study was carried out between March 2014 and November 2014, as a forerunner to a, larger randomised controlled trial (Development and clinical trials of a new Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons-SENATOR www.senator-project.eu) in six hospitals across Europe. The sites included:

(i) Cork University Hospital, Ireland

(ii) Ghent University Hospital, Belgium

(iii) Hospital Universitario Ramón y Cajal, Spain

(iv) Landspitali University Hospital Reykjavik, Iceland

(iv) Aberdeen Royal Infirmary, Scotland

(vi) Ospidale Riuniti, Ancona, Italy

As per the SENATOR trial protocol, patients over the age of 65 presenting to the emergency department with an acute illness, ≥ 3 chronic medical disorders and not under the care of a geriatrician were eligible for inclusion in the study within 72 hours of presentation to the emergency department. Exclusion criteria included, elective hospitalisation, direct admission to intensive care unit and documented plan for consultation with geriatric medicine. All patients signed a consent form after they were informed and appraised of the study and its aims. In the case of patients with cognitive impairment, proxy consent from their next of kin was sought.

7.2.2 Application of SHiM

As part of the SENATOR trial, a case report form (CRF) was completed for each recruited patient. The CRF systematically collected data on patients' demographics, living arrangements, medical history, medications history, as well as several tests assessing their overall health. SHiM was one component of the CRF.

A modified version of SHiM consisting of 18 questions was used to obtain accurate drug histories for patients in phase 1 of the trial, an observational only phase. **Table 7.1** lists the questions asked. Researchers conducted a structured interview with patients within 72 hours of arrival to the emergency department, or in the case of cognitive impairment, this interview was conducted with a reliable care-giver. SHiM was applied after the attending physician had obtained a medication history via the standard methods i.e patient reports, patients' own medications brought to hospital, general practitioner records and/or community pharmacy records. As this was part of an observational phase of the SENAOTR trial, the findings from SHiM were not relayed to the medical team.

Table 7.1: Modified Structured History taking of Medication use (SHiM) questionnaire

General questions	
1.	Are you using your medication as prescribed (dosage, dose, frequency, dosage form)?
2.	Are you experiencing any side effects?
3.	What is the reason for deviating from the dosage, frequency, dosage form or for not taking the medicine at all?
4.	Are you using any other prescription drugs that are not mentioned on this list?
5.	Are you using non-prescription drugs?
6.	Are you using homeopathic drugs or herbal medicines (especially St. John's wort)?
7.	Are you using drugs that belong to family members or friends?
8.	Are you using any "as needed" drugs?
9.	Are you using drugs that are no longer prescribed?
Questions concerning the use of medicines	
10.	Are you taking your medication independently
11.	Are you using a dosage system?
12.	Are you experiencing problems taking your medication?
Difficulties with medications	
13.	In case of inhalation therapy: What kind on inhalation system are you using?
14.	Are you experiencing any problems using this system?
15.	In case of eye drops: Are you experiencing any difficulties using the eye drops?
16.	Do you ever forget to take your medication? If yes, which medication? Why? What do you do?
Other	
17.	Do you have any drug allergies? If yes, specify the drugs/drug classes and symptoms of the allergy.
18.	Do you have any drug intolerances? If yes, specify which drugs/drug classes and symptoms of the intolerance.

7.2.3 Outcomes

Discrepancies (any difference between the medication list obtained by the physician via standard methods and SHiM) were classified into omission discrepancies (drugs identified by SHiM but did not appear on the prescription), commission discrepancies (drugs added to the prescription but not used by the patient, as revealed by SHiM), dose/frequency discrepancies and substitution discrepancies (a drug changed to another drug in that class). Both prescription and non-prescription drugs were included.

Two clinical pharmacists separately classified the potential clinical relevance of the discrepancies using the classification system put forward by Cornish *et al.* [298] and used by Drenth-van Maanen *et al.* in their study [300].

- Class 1 discrepancies were unlikely to cause patient discomfort or clinical deterioration, such as omission of non-prescription vitamins.
- Class 2 discrepancies had the potential to cause moderate discomfort or clinical deterioration, such as diarrhoea, nausea, or moderate pain (solved by paracetamol).
- Class 3 discrepancies had the potential to result in severe discomfort or clinical deterioration, such as gastro-intestinal bleeding, sedation, anaphylactic shock, or severe pain (not solved by paracetamol).

Cases of disagreement were resolved by discussion until consensus was reached.

All potential ADEs experienced by patients during their hospital stay were thoroughly documented, as per the SENATOR trial protocol. The reports of these events were used to determine if discrepancies in patients' medication histories, as revealed by SHiM, resulted in actual clinical consequences.

7.2.4 Data analysis

Statistical analyses were performed in IBM SPSS Statistics version 22. Descriptive statistics were applied to summarise the baseline characteristics, and to describe the number and type of discrepancies.

Ethics approval for this study was sought from and granted by the Clinical Research Ethics Committee, University College Cork as part of the SENATOR trial (Appendix XVII).

7.3 Results

SHiM was applied to 123 patients from 5 of the 6 sites. One of the sites (Ancona) had not begun recruiting at the time of this study. The mean age of the participants was 78 (±6 years). 73 (59%) were male. The median number of medications per patient was 11 (IQR=10.0-14.0). **Table 7.2** summarises the participant characteristics.

Table 7.2: Characteristics of the patients (N=123)

Character	Value
Age (±SD)	78 (±6)
Number of men (%)	73 (59)
Number of women (%)	50 (41)
Median number of medications per patient (IQR)	11 (10.0 – 14.0)
Median number of prescription medications per patient (IQR)	10 (8.0 – 13.0)
Median number of non-prescription medications per patient (IQR)	1 (0.0 – 2.0)
Number of patients from:	
Ireland	68
Iceland	13
Spain	18
UK	21
Belgium	3

IQR = Interquartile range

200 discrepancies between the medication list obtained by the attending hospital doctors and the list obtained by the researcher using SHiM were discovered. Ninety patients (73%) had at least one discrepancy with a median of 1.0 discrepancies per

patient (IQR=0.00-2.25). Of the 200 discrepancies, 132 (66%) related to non-prescription drugs (mostly over-the-counter analgesia, laxatives and antacids) while 68 (34%) related to prescription-only drugs (mostly inhaled bronchodilators, methylcellulose-based eye drops, anti-hypertensives and anti-depressants). Omissions were the most common discrepancy with a total of 131 (65.5%). **Table 7.3** summarises the findings of SHiM.

Table 7.3: Number and type of discrepancies revealed by SHiM

	Total
Number of patients with ≥ 1 discrepancy (%)	90 (73%)
Median number of discrepancies per patient (IQR)	1 (0.0 – 2.25)
Total number of discrepancies	200 (131 prescription only drugs and 68 non-prescription drugs)
Number of omission discrepancies (%)	131 (65.5)
Number of commission discrepancies (%)	28 (14)
Number of dose/frequency discrepancies (%)	32 (16)
Number of substitution discrepancies (%)	9 (4.5)

IQR – Interquartile range

The 200 discrepancies were classified into 3 different categories, as per Cornish *et al.* [298]. Fifty-three (26.5%) were classified as class 1 (unlikely to cause patient discomfort or clinical deterioration), 145 (72.5%) as class 2 (potential to cause moderate discomfort or clinical deterioration), and 2 (1%) as class 3 (potential to cause severe discomfort or clinical deterioration).

Adverse events experienced by patients were examined to determine if they resulted from medication history discrepancies. Of the 123 patients, 19 experienced a total of 33 ADEs. Of these ADEs, 2 were judged to have been a direct result of discrepancies as revealed by SHiM. Both ADEs related to development of marked constipation. One was due to omission of a laxative for a patient taking an opioid analgesic. The second was due to alverine being prescribed three times daily, when the patient only took it periodically when required at home.

7.4 Discussion

The principle findings from this study are as follows:

(i) At least one discrepancy between the medication list obtained by the physician and that obtained by the researcher using SHiM was found in almost three quarters of patients' prescriptions (73%)

(ii) Two thirds of these discrepancies were due to non-prescription drugs, and the majority were omission discrepancies.

(iii) The majority (72.5%) of discrepancies were judged to have potential to cause moderate discomfort or clinical deterioration

(iv) Only 2 (1%) discrepancies resulted in actual clinical consequences.

These findings in part correlate with the limited amount of data in the literature, while also generating novel discussion points. Discrepancies were found in the majority of patients' prescriptions as per previously reported findings [293, 294, 296, 301, 313], although the median number of discrepancies per patient in this study was lower (1.0 compared to 3.0 [300]). The majority of discrepancies were omissions, and had potential to cause moderate discomfort or clinical

deterioration, similar to previous findings [300, 313]. Most studies to date have not explored the link between medication history discrepancies and actual adverse events [313]. Also, many have not included non-prescription medicines [300]. Drenth-van Maanen *et al.* did account for these and reported that 21% of patients experienced actual clinical consequences as a result of medication history discrepancies. Thirty-four percent of discrepancies in that single centre study were due to non-prescription medicines [300]. However, in the present study, less than 2% of patients experienced clinical consequences as a result of discrepancies, while non-prescription medicines accounted for 66% of all discrepancies.

The large difference in proportions of patients experiencing consequences as a result of discrepancies is curious. It could possibly relate to the proportion of discrepancies caused by non-prescription medicines. It is possible that over-the-counter medicines are less likely to cause symptomatic adverse events within a short period of time. This would explain the small numbers of patients developing ADEs in the present study given that the majority of discrepancies were related to non-prescription medicines. By contrast, in the study by Drenth-van Maanen *et al.* the vast majority of discrepancies were caused by prescription-only medicines. However, even though most patients in the present study did not experience discrepancy-related ADEs, most discrepancies were judged to be clinically relevant with potential to cause harm. This demonstrates the importance of accurately recording non-prescription as well as prescription drugs in a medications reconciliation.

The results clearly reinforce the message proposed by previous studies that a structured history taking optimises the medication reconciliation process and elicits more information than standard methods. However, they do not suggest that SHiM could actually prevent avoidable ADEs to a large extent. Ninety-nine percent of the ADEs which patients experienced would not have been prevented by the application of SHiM. However the fact that almost 75% of discrepancies had the *potential* to cause moderate discomfort or clinical deterioration indicates that SHiM does have a place in optimising prescribing for older patients. Applying structure to the medications reconciliation process is undoubtedly logical and beneficial, as illustrated in this study and similar studies in the literature [300, 313, 317, 318]. Typically, medication histories taken by different health care professional vary in terms of quality and thoroughness [313, 319]. However with a structure for medication reconciliation in place, not only is the resultant medication list more accurate, but the medications reconciliation can be completed to the same standard by doctors, nurses and pharmacists [300].

While SHiM revealed discrepancies in patients' prescriptions, it must be remembered that it is unlikely that all these were unintentional. Doctors often initiate/discontinue medications, adjust doses or substitute medications on admission to hospital based on their clinical assessment of the patient. The 200 discrepancies identified in this study therefore may not be a true reflection of how many *unintentional* discrepancies were present. As with previous studies, the small sample size in this study limits the generalizability of the results, although the range of countries involved is a strength of the study.

The overall evidence for using SHiM is mixed and further research is needed, with larger cohorts, to clarify the role of SHiM in the optimisation of older patients' prescriptions. First and foremost, SHiM is a tool to optimise medications reconciliation. The results presented here and elsewhere indicate that SHiM achieves this aim. Whether it can serve as an ADE preventative is less certain.

7.5 Limitations

This study was limited to 123 patients. While this is a larger sample size than previous studies examining SHiM [300], it is still small and studies using larger cohorts are required.

One of the sites involved in the SENATOR project had not begun recruiting at the time of this study therefore no data was available.

While it is useful to collect data from several international sites, it also introduces a problem in terms of variability. Each site had researchers of different professions and backgrounds collecting the data which may lead to differing interpretations of data. There was also much variation in the numbers of patients recruited from each site, making direct comparisons between countries impossible.

Since much of the SHiM tool involves researchers' own interviewing skills, the validity and reliability of the total data set is questionable given the broad range of experience amongst the researchers.

7.6 Conclusion

The use of SHiM to obtain medical histories for 123 patients revealed 200 discrepancies from the list obtained by the attending physician. The majority of

these discrepancies were due to non-prescription drugs, and most were omissions discrepancies. However, only two of these discrepancies resulted in actual adverse drug events. The results indicate that SHiM is an effective medications reconciliation tool. However, further research applying SHiM in larger populations of older people in a variety of clinical settings is required to assess its ability to contribute to ADE prevention.

8. A meta-synthesis of potentially inappropriate prescribing in older patients: An update

Chapter description

The meta-synthesis described in chapter 2 analysed studies published up to and including April 2013. It was timely therefore to perform another search of the literature and update the findings.

8.1 Introduction

In chapter 2, qualitative studies exploring the causative factors of PIP were synthesised using meta-ethnographic methodology [171]. This meta-synthesis identified four key concepts that reflected the findings in the chosen papers as being contributory factors to PIP in older patients, namely:

(1) Desire to please the patient

(2) Feeling of being forced to prescribe

(3) Tension between experience and guidelines and

(4) Prescriber fear

It was concluded that, in many situations, prescribers suffer from 'self-perceived restrictions' leading to a sense of powerlessness to prescribe appropriately for older patients. This forces them to rely on what they know and have done before, leading to the PIP that has been identified [11, 17, 41, 52, 165].

The meta-synthesis in chapter 2 included papers up to and including April 2013. The aim of this chapter therefore, is to update the search using papers published since then, and adjust the findings accordingly.

8.2 Methods

As in chapter 2, the meta-ethnographic process, as described by Noblit and Hare [171] was utilised to synthesise suitable papers. This process is described in detail in chapter 2 and was implemented in identical fashion for this chapter. **Figure 8.1** illustrates the process.

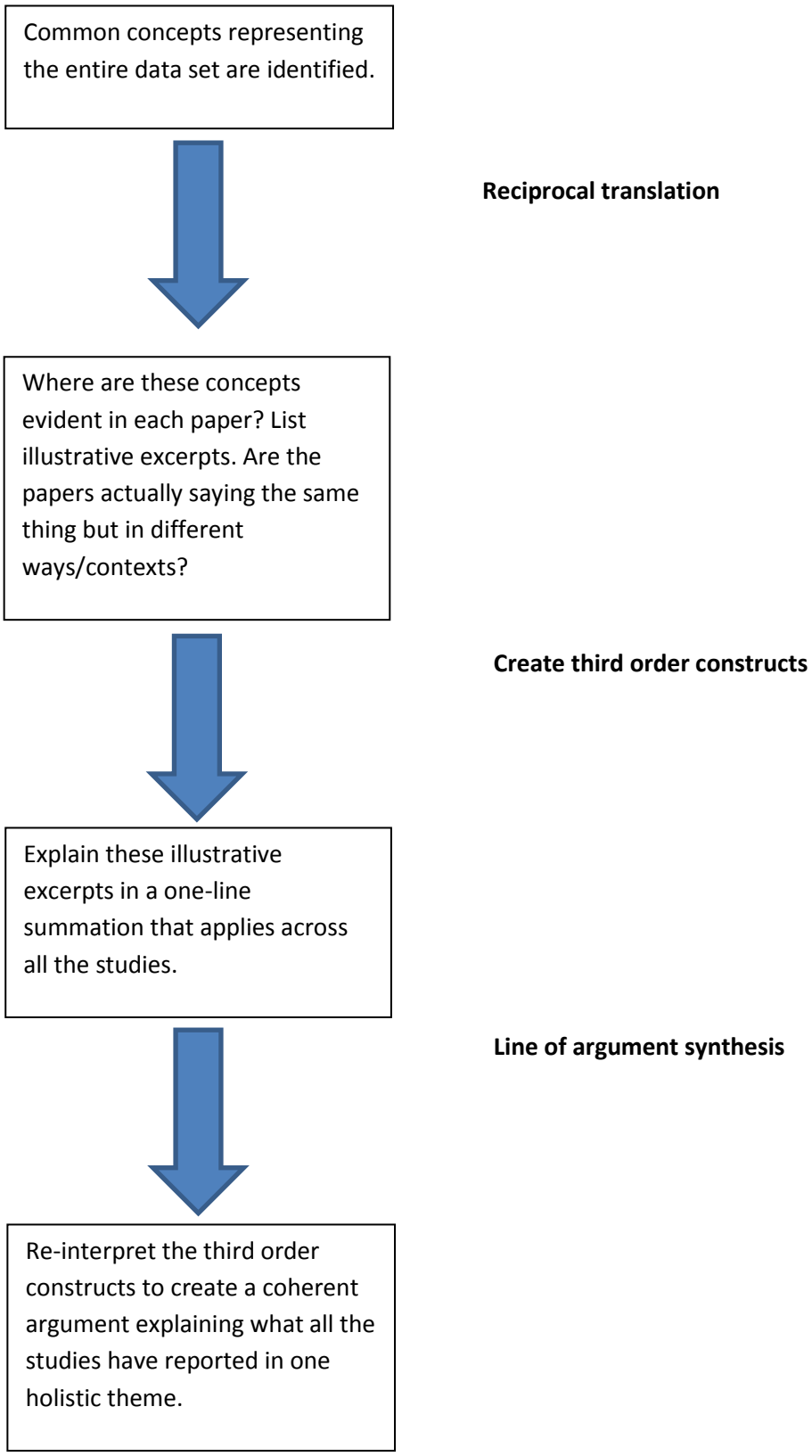


Figure 8.1: Flow diagram of meta-ethnography process

8.3 Results

The search of the electronic databases identified 151 papers, leaving 58 after duplicates were removed (**Figure 8.2**). After title and abstract review, a further 50 were removed: 41 did not use qualitative methods, 4 did not involve PIP, 3 did not deal with patients over 65 and 2 had no abstracts available. Eight full papers were retrieved for review. Of these, 5 were eliminated. Three did not use qualitative methods and 2 did not explore causative factors of PIP. This left 3 papers for inclusion in final synthesis (**Table 8.1**).

All 3 papers were of high quality when assessed using the CASP criteria; each of the papers met most of the criteria for inclusion in the analysis. Common weaknesses were:

(1) Discussion around the contribution of the findings to current knowledge.

(2) 'Reflexivity' (the awareness of the *researcher's* own contribution to the construction of meanings throughout the research process).

(3) Examination of the relationship between the researcher and the participants.

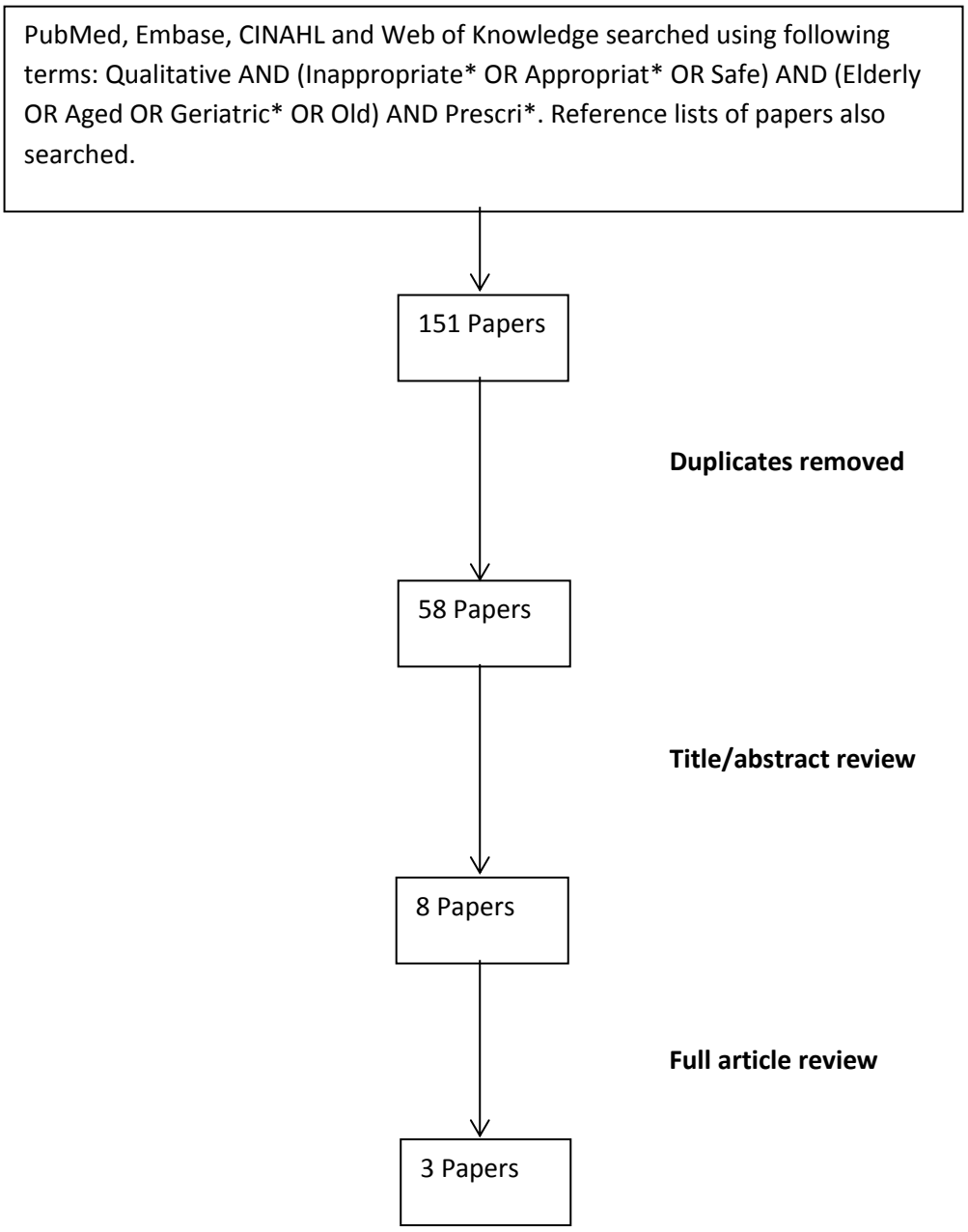


Figure 8.2: PRISMA flow diagram of literature review process

Table 8.1: Characteristics of papers identified

	Paper title (year of publication)	Authors	Country	Sample size	Methods
1	Factors influencing prescribing of fall-risk-increasing drugs to the elderly: A qualitative study (2015)	Bell *et al.* [320]	Norway	13 GPs	Systematic text condensation . Semi-structured focus groups.
2	Doctors' perspectives on the barriers to appropriate prescribing in older hospitalised patients: A qualitative study (2014)	Cullinan *et al*.[215]	Ireland	22 Hospital doctors	Framework analysis. Semi-structured interviews
3	GPs, medications and older people: A qualitative study of general practitioners' approaches to potentially inappropriate medications in older people (2015)	Magin *et al.* [321]	Australia	22 GPs	Thematic analysis. Semi-structured interviews

GP=General practitioner

8.3.1 Reciprocal translation

Four key concepts that reflected the findings in the 3 papers were identified from the meta-synthesis as being contributory factors to PIP:

(1) Patient influences

(2) Quality of life versus prescribing guidelines influencing decision making

(3) Working environment

(4) Lack of prescriber knowledge

The reciprocal translation and final synthesis are presented below. Each of these thematic concepts are described in greater detail. Excerpts consisting of original quotes from participants (first order constructs) as well as authors' findings (second order constructs), from the original papers are presented in table 8.2 along with third order interpretations to illustrate how the four themes were identified.

Patient influences

As in Chapter 2, there was a clear theme of wanting to please the patient amongst the three papers identified in this search. While prescribers were aware that their prescriptions were often potentially inappropriate, patients demands and preferences often led to potentially inappropriate medications (PIMs) being prescribed anyway. Magin *et al.* described the difficulty in stopping benzodiazepines.

"*Each time you try and broach it with them* [benzodiazepine cessation] *you do the same dance and end up back at the same spot".* **(Respondent 6)** [321]

Bell *et al.* reported that prescribers find it 'unpleasant to say no' when asked ny patients to renew their sleeping pills prescription. Their study found that doctors tired of saying no even though they knew the potential adverse effects of these drugs.

"Many patients are very fond of their drugs and are very reluctant to end the treatment. Then my threshold to let them continue is often low". **(Female GP, 11 years of practice)** [320]

Cullinan *et al.* [215] echoed these sentiments describing the pressure prescribers feel to prescribe something they know is not appropriate.

"As a doctor sometimes you feel that you have to do something, you get pressurised by relatives or patients. You have to give them something. So you end up giving something that you are not 100% happy with". **(Site 2, interview 2, registrar).** [215]

Quality of life versus prescribing guidelines influencing decision making

Each of the 3 papers highlighted the conflict that exists between common prescribing guidelines and prescribers' decision making processes. One common theme was that the guidelines are not suitable for older patients as this population react so differently to drugs. Therefore what the guidelines deem 'inappropriate' may be true for one patient but not for the next. Prescribers reported treating patients on a case-by-case basis and if they thought stopping a medication according to the guidelines would impact on the patient's quality of life, they would more often than not continue with the current treatment.

"All trials are a sort of pooled data situation, and there will be individuals for whom a particular medication works well and may still be appropriate. I think we deal with an individual and a person sitting in front of us and try and juggle things…I don't think they [guidelines like the Beers criteria] *should ever be rigid ones because that doesn't fit reality".* **(Respondent 1)** [321]

Bell *et al.* reported that prescribers feel guidelines 'do not reflect the complexity in primary care' and that 'elderly people with polypharmacy and multiple diseases are very different from the population the guidelines are based upon'. This leads to GPs continuing to prescribe medications that technically may be classified as inappropriate. 'The GPs would continue to prescribe fall risk increasing drugs (FRIDs) if they perceived that termination of that medication would negatively impact the patient's quality of life' [320].

Quality of life compared to prescribing guidelines also emerged as a causative factor of PIP in the study by Cullinan *et al.* 'Doctors did however say that they did not think their choices were putting their patients at risk after weighing the risks and benefits and that quality of life was a major deciding factor' [215].

Working environment

The environment in which doctors prescribe was reported as a contributory factor to PIP is some manner in all 3 papers. It was referred to in terms of doctors' workloads, resources available, demands on their time from multiple sources and interactions, or lack thereof, between the different levels of care. All were said to lead to the prescribing of PIMs.

For example, Bell *et al.* described how GPs felt that older patients often present with multiple issues therefore reducing the amount of time available to review their medications. This often resulted in prescriptions just being renewed without a critical assessment of appropriateness.

"If he struggles with his sleep that is only one of many problems. I do not arrange a new appointment to just talk about his drugs. That will be a complication for both him and me". **(Male GP, 9 years in practice)** [320]

The same study also highlighted the availability of electronic prescribing systems to prescribers as beneficial in terms of 'improving the possibility of gaining an overview of the patient's drug use and also of preventing over-prescribing and misuse'.

Cullinan *et al.* showed that the busy environment in which hospital doctors work was a probable contributing factor to PIP in older patients.

"That's a major problem. What you want to do when writing out a drug kardex [prescription chart] *is to be on your own, to be left alone for 5 minutes…..But it's actually an ideal opportunity for anybody who wants a piece of you for advice or whatever…nobody respects that at all and nursing staff will use it as an opportunity to unload multiple other problems".* **(Site 1, Interview 6, Intern)** [215]

In the same study, lack of information technology (IT) infrastructure was reported as a further contributory factor to PIP. 'Interviewees noted that improvements in the IT infrastructure could lead to much safer and more appropriate prescribing,

with many doctors emphasising that prioritising improvement initiatives around IT could have the most significant effect on appropriateness of prescribing'. [215]

Magin *et al.* described the lack of communication between levels of care as being a contributory factor to PIP. Specifically, if a medication is started by a specialist, there is a reluctance by the patient's GP to change it, or even to contact the specialist to discuss it. As a result, the GP renews a prescription for something that he/she may feel is not appropriate [321].

"Potentially inappropriate medications may be prescribed by a specialist….it's a bit difficult….being a GP to then say 'well, I don't think I want that'". **(Respondent 11)** [321]

Lack of prescriber knowledge

All 3 papers reported prescribers' lack of geriatric pharmacotherapy as a potential cause of PIP in older patients. Most participants recognised the older population as being very different to the general adult population and acknowledged the extra demands their care requires. However, not all had the knowledge base to prescribe appropriately for older patients. Magin *et al.* showed that 'the anticholinergic effects on cognition of some PIMs were not universally appreciated' [321].

"I know it [propantheline] can cause dry mouth and things like that…..and the constipation but I was unaware of cognitive effects in a patient with dementia". **(Respondent 8)** [321]

Magin *et al.* also reported that none of the participants were aware of the Beers criteria [321].

Cullinan *et al.* showed that doctors often feel they are not well equipped to prescribe appropriately for older patients due to 'a lack of specific education and training in geriatric pharmacotherapy, and also a lack of communication of clinically relevant information with regards to older patients' [215].

"I don't think there is enough training for prescribing in older patients. There is no distinction between older patients and the general adult population in the training". **(Site 4, Interview 2, Registrar)** [215]

Again, none of the participants in this study (except consultants) were aware of any screening tools for PIP in older patients such as Beers Criteria [63] or STOPP/START criteria [69, 70].

Bell *et al.* described how GPs did not associate increased risk of falls with certain inappropriate medications [320].

"To be honest I believe it is the sum of many factors like alcohol, domestic traps, multiple diagnoses and bad quality of life that makes them fall". **(Male GP, 10 years of practice)** [320]

The authors described how 'GPs did not consider drug use to be an important enough risk factor for falls in general to let it affect their habit of renewing prescription of 'fall risk inducing drugs' (FRIDs) without performing regular drug reviews' [320]. They indicated that this is in contrast to research findings which suggest that use of FRIDs is in fact associated with increased risk of falls. They concluded that 'GPs need to be reminded of this connection and that the patient's drug list needs to be assessed for such instances [320].

Table 8.2: Excerpts supporting the four themes plus third order interpretations

	Excerpts (first and second order constructs. First order constructs in italics)	Paper(s)	Third order interpretations
Patient influences	*"It might be our bad consciences that make it easier to write a prescription. Most patients are more satisfied if they get one"*	Bell *et al.* [320]	Doctors are aware that sometimes they prescribe medications which are potentially inappropriate. However, there is a sense of fighting a losing battle at times with patient demands and patient satisfaction guiding prescribing rather than prescribing guidelines
	The majority of doctors admitted that patients and/or their families can influence their prescribing to the point where they prescribe something they are not totally happy with.	Cullinan *et al.*[215]	
	"I would like to think we never prescribe something we know is wrong but there's no doubt it sways you where it's a grey area"	Cullinan *et al.*[215]	
	"Each time you try and broach it with them [benzodiazepine cessation] *you do the same dance and end u[p back at the same spot"*	Magin *et al.*[321]	
	"When people first come, I don't usually go OK well we need to stop this, this and this. I mean, you've got to gain some sort of confidence that you know what you are doing".	Magin *et al.*[321]	
Quality of life versus prescribing guidelines influencing decision making	The GPs would continue to prescribe FRIDs if they perceived that termination of that medication would negatively affect the patient's quality of life	Bell *et al.* [320]	Guidelines cannot be applied unequivocally across the board in older patients. An individualised approach must be taken which can at times result in medications which would technically be classified as inappropriate being prescribed,
	Doctors did say they did not think they were putting their patients at risk and that quality of life was always a major deciding factor.	Cullinan *et al.*[215]	
	Initiation or continued prescription in any individual scenario	Magin *et al.*[321]	

Table 8.2 Contd

	was found to be a result of a reasoned weighing of harms and benefits. *"You've got a description from the patient, an idea of how big the problem is, we don't expect the drugs to bee completely safe, we're trying yo weigh up whether the risks are justified by the size of the benefit we're looking for".*	 Magin *et al.*[321]	
Working environment	A pull factor that could initiate change in prescribing of FRIDs and other drugs was the electronic prescription system. The GPs said that time set aside for consultations affected prescribing. *"I do think though, it's a tough job. It really is very tough, you're just flat out busy all the time. I think a lot of times you're just transcribing things. You go into auto pilot and you don't question it".* Another frequent scenario was of PIMs initiated by specialists. GPs felt that these were very difficult for them to cease.	*Bell et al.*[320] Bell *et al.*[320] Cullinan *et al.*[215] Magin *et al.*[321]	Several factors in a doctor's working environment contribute to PIP. Heavy workloads, lack of time, lack of resources and lack of communication between levels of care all create an environment conducive to PIP.
Lack of prescriber knowledge	*"I find it easier to remove antihypertensive medications compared to psychotropic drugs since I better understand the pharmacological correlation between the effect of the drug and the symptom of dizziness"* Participants noted a lack of specific geriatric pharmacotherapy training and a lack of communication of clinically relevant information.	Bell *et al.*[320] Cullinan *et al.*[215]	Lack of specific geriatric pharmacotherapy training results in doctors being unequipped to prescribe appropriately for older patients.

Table 8.2 Contd

	"It's a different knowledge set. And it's difficult you know because there isn't a huge amount of data out there, or its not communicated to us very well"		
	GPs were generally unaware of the Beers criteria.	Magin *et al.*[321]	
	The anticholinergic effects on cognition of some PIMs were not universally appreciated.	Magin *et al.*[321]	
	Few respondents identified additive anticholinergic effects of different medications as being something that they considered in prescribing in older perrsons.	Magin *et al.*[321]	

8.3.2 Line of argument synthesis

In Chapter 2, a line of argument synthesis was proposed, stating that in many situations, prescribers suffer from 'self-perceived restrictions' leading to a sense of powerlessness to prescribe appropriately for older patients. This forces prescribers to rely on what they know and have done before, which leads to the high prevalence rate of PIP that has been identified [11, 17, 41, 52, 165]. Examining the concepts identified in this updated search, the same line of argument synthesis appears to hold true. Patient demands, perceived lack of appropriate guidelines, working environments conducive to inappropriate prescribing and lack of geriatric pharmacotherapy knowledge all serve to render the prescriber powerless to prescribe appropriately and diminish any incentive for change.

8.4 Discussion

While presented differently at times, all 4 concepts identified in Chapter 2 were present in this updated search of the literature. 'Desire to please the patient' was directly related to 'patient influences', as was 'feeling of being forced to prescribe'. 'Tension between experience and guidelines' was directly related to 'quality of life versus prescribing guidelines influencing decision making'. The theme of 'prescriber fear' was evident in several places. For example, in 'patient influences' there was a fear of disrupting a patient's care by stopping a medication when they had been taking it for a long time. In 'lack of prescriber knowledge' there was fear of stopping a patient's medications due to lack of understanding of pharmacological correlation between the effect of the drug and the potential for adverse effects.

A new concept arising out of this search was that of the working environments of doctors being a contributory factor to PIP. Although not evident in chapter 2, this factor seems likely given the generally large workloads of doctors today, and therefore is a logical addition to the findings of this research.

As a result, while the various strategies suggested in chapter 2 to empower physicians to prescribe appropriately still hold true, this update has highlighted that changes to the environment in which doctors work are also required. This includes making the necessary resources available, allowing doctors sufficient time to review patients' medications and improving communication between levels of care.

Another point of note arising from this update is the dissatisfaction with current guidelines with regard to prescribing for older patients. In chapter 2, participants expressed frustration arising from inability to implement the guidelines due to external pressures. However, the participants in this updated search argue convincingly that most prescribing guidelines are not designed specifically for older patients and therefore cannot be applied effectively to this population. However, in all 3 papers in this review, very few of the participants were aware of Beer's criteria, one of the primary tools available for assessing older patients' prescription for appropriateness. Therefore, while their arguments may hold true with respect to generic prescribing guidelines, the question must be asked why they are not aware of the tools available that are in fact designed for use in older patients. This points towards another clear area for future intervention.

8.5 Limitations

Although suitable papers were systematically searched for, qualitative papers are often difficult to find due to ambiguous titles.

Meta-ethnography, while a useful tool for this kind of research, is not an objective technique and is open to differing interpretations between different researchers.

I was the one of the researchers who read all the papers. Given that one of the papers included was my own publication, it introduces an element of bias, which potentially affects the reliability of the findings.

8.6 Conclusion

The concepts identified in Chapter 2 remain relevant after this updated search. However, an additional concept has beeen identifed. Doctors' working environments currently contribute to PIP due to lack of resources, strains on doctors' time and lack of communication between levels of care. These issues, as well as others raised here and in chapter 2 will need to be addressed in future interventions to address PIP.

9. Thesis Discussion

9.1 Summary of findings

The first novel outcome of this thesis, leading to two publications in peer-reviewed journals, was the exploration of the causative factors of PIP and related outcomes through qualitative research. The first step in this process was a systematic review of existing qualitative literature (meta-synthesis) exploring PIP (Chapter 2) [156]. There is debate as to the appropriateness of combining qualitative studies in a formal synthesis like this and whether different types of qualitative studies using different methodologies should be combined [322]. Recent investigation suggested that it is difficult to draw firm boundaries around what is, and is not, a particular type of qualitative research as many authors fail to clearly define their methodologies [322]. Despite this, the same investigation also found that it is possible to synthesise across different traditions such that some researchers consider the combining of data from multiple theoretical and methodological traditions a strength of the review [323].

The meta-synthesis identified four key concepts as being contributory factors to PIP. They were:

(i) **Desire to please the patient.** In the majority of papers, there was a clear underlying theme of 'wanting to please the patient'. This usually meant prescribing outside common guidelines. Doctors recognised the problem of prescribing PIMs, however, due to some patients' resistance to alternative therapies, they proceeded with prescribing the medication anyway (Chapter 2, p38).

(ii) **Feeling of being forced to prescribe**. One consequence of this need to please the patient was that prescribers often felt they were forced into prescribing, or not prescribing medications, in a manner they knew did not adhere to guidelines. However there were other factors leading to prescribers feeling forced to prescribe e.g. poor quality of treatment resources and lack of alternative therapies (Chapter 2, p40).

(iii) **Tension between experience and guidelines.** Physicians perceived a significant problem with implementing prescribing guidelines in day-to-day practice. The end result was reversion to previous practises, and what they were familiar with. Lack of evidence supporting some guidelines also influenced prescribers in favour of his/her own experiential evidence (Chapter 2, p41).

(iv) **Prescriber fear.** Doctors felt a sense of fear towards older patients in general due to their frailty and co-morbidities. Consequently, they perceived more potential to do harm. They also observed a fear of the unknown amongst several GPs (Chapter 2, p42).

The update of the search, presented in Chapter 8, identified one further theme i.e. the working environment of prescribers being conducive to PIP. This included factors such as time constraints, lack of resources for non-drug therapies and lack of communication between levels of care (Chapter 8, p161).

These findings correlate well with another recent meta-synthesis exploring causative factors of PIP from the prescribers' perspective [324]. In this study, Anderson *et al.* identified 4 analytical themes contributing to PIP, namely:

(i) **Problem awareness**. Poor insight into PIP was observed throughout the papers selected for the meta-synthesis.

(ii) **Inertia.** Inertia is defined as the failure to act, despite awareness that prescribing is potentially inappropriate, because discontinuing PIMs is perceived to be a lower value proposition then continuing PIMs. Factors such as fear of unknown/negative consequences of change, downplaying risk of harm and delegating responsibility to another party (another prescriber) all contributed to this theme.

(iii) **Self-efficacy.** This theme refers to factors that influence a prescriber's belief and confidence in his/her own ability to address PIM use. Knowledge or skill deficits, including difficulty in balancing the benefits and harms of therapy, recognising adverse drug effects and establishing clear-cut diagnoses/indications for medicines, were challenges prescribers faced in identifying and managing PIMs.

(iv) **Feasability.** This refers to factors, external to the prescriber, which determine the ease or likelihood of change. The most frequently expressed barrier to PIM avoidance was patients' ambivalence or resistance to change and their poor acceptance of alternative therapies. The limited time and effort to review and discontinue medications was

another common constraint as was the limited availability of effective non-drug treatment options.

Although labelled differently, all the above themes from Anderson *et al's*. study are identified to some extent in the meta-synthesis presented in Chapters 2 and 8 of this thesis. The similarity between the findings strengthens the argument for both studies' conclusions i.e PIP is a result of both external and internal factors affecting prescribers' decision making. A multi-faceted approach to minimising PIP is clearly needed. This includes more comprehensive education with greater emphasis on de-prescribing and system-level interventions that empower physicians to prescribe appropriately is required to address each area identified by this research.

To further explore the causative factors of PIP, and given the lack of qualitative research in the field highlighted in Chapter 2, an empirical qualitative study was carried out and is presented in Chapter 3. Analysis of 22 semi-structured interviews with hospital doctors of varying grades using the TDF (Appendix V) identified 5 domains as relevant to minimising PIP (Chapter 3, p67). They were:

(i) Environmental context and resources,

(ii) Memory/attention and decision processes,

(iii) Knowledge,

(iv) Skills,

(v) Social influences.

These findings largely concur with the findings of the literature review i.e a mixture of external factors (working environment, patient influences and lack of resources) and internal factors (lack of knowledge and confidence with regards to geriatric pharmacotherapy) combine and ultimately result in PIP. Of particular note in this study, more so than in the literature review, was participants' dissatisfaction and frustration with current IT infrastructure in Irish hospitals, especially with regards to patient transition between levels of care. Improved IT resources was commonly suggested as factor likely to improve prescribing in older patients.

Lack of specific geriatric pharmacotherapy training was also seen as a contributory factor to PIP. Doctors indicated that they often feel ill-equipped to prescribe appropriately for older patients. This deficiency was not only their technical knowledge, but also, it would seem, in their interactions with these patients and their families. Doctors reported being frequently influenced in their decision making by patient demands/preferences. This usually meant prescribing drugs they knew to be potentially inappropriate. This would suggest that doctors' training should incorporate some level of guidance on dealing with patients' and families' treatment demands, and being able to resist these demands when necessary and in patients' best interests. Recently, Gordon *et al.* recognised this need and has proposed a template for such pragmatic training [185, 325].

The findings from Chapter 3 shed new light on the causative factors of PIP. In 2005, Spinewine *et al.* explored the processes leading to PIP in older inpatients using qualitative methods [180]. They identified transition between levels of care as a contributing factor to PIP. In addition, lack of disparity between prescribing trends

for older adults and the younger adult population and lack of time to prioritise medication appropriateness were also contributory factors to PIP. However, their findings with regards to the attitudes of prescribers differ significantly from those presented in Chapter 3. They reported that prescribers adopted a passive attitude towards learning, expressing a view that it would take too long to find the information they needed about medicines. They also described a lack of self-directed learning amongst the doctors they interviewed [180].

In contrast, some of the study findings described in Chapter 3 were the converse of those of Spinewine *et al*. i.e doctors were very interested in learning more because they felt they hadn't been taught enough as undergraduates and welcomed any opportunity to enhance their knowledge base. Spinewine *et al.* also described the relationship between the prescriber and the patient as a paternalistic one, with the prescriber making the decisions without due consideration of the patient's wishes. This, they found, contributed to PIP [180]. Once again, the study presented in Chapter 3 had opposite findings with doctors allowing themselves to be influenced by patients' demands often resulting in PIP. It is likely that elements of both studies combine to cause PIP. The profile of the participants in both studies must also be considered. Spinewine *et al.* interviewed nurses and pharmacists as well as doctors. Chapter 3 only involved interviews with doctors thereby applying a narrow focus. However the difference in attitudes, identified by this thesis, between Ireland and mainland Europe may be an area for future research.

The second novel outcome of this thesis was, using the findings of the qualitative research, the identification of the types of interventions that would be suitable for

the purpose of preventing PIP and related adverse outcomes. At the end of Chapter 3, the domains identified in the TDF were mapped to the behaviour change wheel (Appendix VI) for this purpose (Chapter 3, p76). The intervention types found to be suitable were:

(i) Training,

(ii) Environmental restructuring,

(iii) Restrictions,

(iv) Persuasion,

(v) Incentivisation,

(vi) Modelling,

(vii) Enablement

These findings provide a roadmap for future research in the field of PIP prevention in secondary care. A similar investigation into suitable intervention types for PIP prevention in *primary* care has recently been published [326]. Although not based on any theoretical model, Clyne *et al.* did use qualitative methods to inform an intervention aimed at preventing PIP. They reported that academic detailing, with a medicines usage review conducted by a pharmacist and patient information leaflets had the potential to reduce PIP in patients under the care of primary care physicians [326]. This intervention, guided by the United Kingdom Medical Research Council (MRC) Framework on developing complex interventions [327] is currently being evaluated in a randomised controlled trial [328].

Of the intervention types identified by their study, two directly overlap with those identified in Chapter 3 of this thesis i.e. academic detailing (training) and medicines

usage review by a pharmacist (environmental restructuring). Patient information leaflets do not fall under any of the intervention types identified in this thesis. However, this is not surprising as the TDF and behaviour change wheel were employed to identify areas for intervention at the *prescriber* level. Nevertheless, patient education was mentioned by participants in the interviews described in Chapter 3 as a potential enabler to appropriate prescribing in older patients. Therefore it would seem that interventions to address PIP will be similar in both primary and secondary care. The fact that the meta-synthesis in Chapter 2 (involving primary and secondary care physicians) and the qualitative study in Chapter 3 (involving secondary care physicians only) produced similar findings supports this view point.

The third novel goal of this thesis was to develop and conduct an intervention informed by the qualitative research, based upon the intervention types deemed suitable by mapping the qualitative research to the behaviour change wheel and suitable for the purpose of countermanding PIP. There was general dissatisfaction among NCHDs with the lack of geriatric pharmacotherapy training they had received as undergraduates. Consequently, there was general agreement among them that improving pharmacotherapy knowledge would be a vital step in countermanding PIP. Therefore, an educational intervention was decided upon (Chapter 4). Specifically, an online module providing geriatric pharmacotherapy and prescribing training. Doctors expressed a general desire for more training, and a view point that it should be delivered in a fashion in which they could complete it in their own time. Given these expressed views, and the fact that 'training' was one of

the intervention types identified by the behaviour change wheel, this intervention seemed appropriate.

The results raise several points of interest. Firstly, the low knowledge scores achieved at baseline are in agreement with doctors' reports of being unequipped to prescribe for older patients due to insufficient training in this area (Chapter 4, Table 4.3, p92). Secondly, the marked improvement in scores post-intervention demonstrates the benefit of a tool like this. Gordon *et al.* have reported similar findings using an online training tool for doctors designed to improve prescribing in children in the UK [221].

As mentioned in the introduction to this thesis, specific educational interventions are often promoted as essential for helping doctors to prescribe appropriately in specific patient groups [52]. Interactive style interventions, such as that described in this thesis, are usually the preferred choice [106-108]. The results from the RCT in Chapter 4 corroborate previous findings as to the value of such interventions. In addition, the data make a strong case for changing the focus of these interventions from single drug classes to prescribing for older people in general with particular emphasis on the physiological changes that occur as patients age. The basics of geriatric pharmacotherapy must be mastered first and this research strongly suggests that these basics are being overlooked in medical education. The reality is that physicians are often prescribing for a patient population for which they have not been adequately trained. Therefore, they often prescribe as they would for a younger adult. Tools like the one used in this thesis could have a central role in the future in preparing doctors for the challenges of geriatric pharmacotherapy,

Especially in Ireland, and other countries, where these educational tools are not routinely available.

The suggestions from the RCT participants put forward for preventing PIP are also noteworthy (Chapter 4, p95). Interestingly, after content analysis of all suggestions, the 3 overarching themes were:

(i) Supplementary training in Geriatric Medicine with more emphasis on the differences between older patients and the general adult population in relation to drug choice and dose selection,

(ii) Improved IT support in terms of transfer between levels of care,

(iii) Improved and more systematic communication between the levels of care i.e GPs, hospitals, pharmacies and nursing homes.

The findings echo those of Chapter 3 and underline what prescribers feel is required to address PIP. The issue of insufficient and inadequate IT support in Ireland, and it's association with PIP is a novel and important finding of this thesis. Research to date investigating the role of IT in prescribing has mainly focused on medication adherence, prescribing accuracy, reducing medication errors and improving efficiency of transition of care [329-332]. A review of studies examining the use of IT in prescribing also described research aimed at using IT to improve overall appropriateness of prescribing in patients with heart failure [330]. The message from this research is similar throughout. Agrawal *et al.* reported that use of electronic systems for prescribing and collating patients' medical records reduces errors, increases overall safety and improves efficiency of transition of care [330].

There are some concerns surrounding these systems however e.g. cost. IT systems are of little clinical value unless all healthcare facilities have the capacity to interact with them. Widespread implementation such as this places a large burden on any institution or organisation [330-332]. The user interface is another commonly reported barrier. There is a danger that prescribers would become frustrated with an electronic system constantly interrupting their workflow [330]. Therefore streamlining of these systems is required to encourage their use.

Several of these IT systems exist abroad in some form, and are showing potential in improving prescribing. In Ireland, the great majority of health records, prescribing and interactions between levels of care are still paper-based. The present research has highlighted prescribers' frustration with this status quo. Something which has not received much attention to date but clearly needs to in the future. Recent large scale European studies involving Ireland, such as the EU FP7 funded SENATOR project and the Horizon 2020 funded project- OPERAM, both focusing on developing software to aid physicians to optimise their prescribing for older patients, are therefore a timely and welcome development (www.senator-project.eu).

The final novel outcome of this thesis, leading to publication in a peer-reviewed journal, was the assessment of other possible intervention types identified in the thesis for suitability and applicability with regards to preventing PIP and related outcomes such as ADRs. This thesis has shown that doctors are not adequately trained in geriatric pharmacotherapy to identify instances of PIP to a sufficiently high level. In addition, doctors are under increasing time pressures and

appropriateness of prescribing is not always a priority. One of the intervention types identified by the behaviour change wheel was 'enablement'. In other words, if one could enable doctors to readily identify patients with instances of PIP, or at least with an increased risk of PIP and related outcomes, it could potentially have a positive effect on PIP/ADR rates.

Given the need for succinct interventions due to the already complex environment doctors work in, it was hypothesised that a single indicator of PIP/ADR risk on the patient's drug chart or medical notes would be beneficial. To do this, a frailty index (FI) was developed and tested, and frailty scores assigned to patient databases in Chapters 5 and 6. Significant correlation between the FI scores and appropriateness of patients' medications indicated that FI scores did have potential to form the basis of such an indicator for physicians to review a patient's medications (Chapter 5, Figure 5.2, p111). Further analysis identified an FI threshold above which patients were statistically more likely to experience PIP/ADRs raising the possibility that such an intervention could be delivered by simply ticking a box if a patient is above this threshold (Chapter 5, Figure 5.3, p113). The findings from Chapter 5 were tested on a different patient set in Chapter 6 and generated strikingly similar results (Chapter 6, Tables 6.2, 6.3 and 6.4, p130-132) thereby adding weight to their significance.

This research has identified a novel use for the FI, a tool which has often generated debate as to how best to utilise it [229, 279, 283]. The study indicates that this is one potential way for patients at high risk of PIP/ADRs to be highlighted to doctors who otherwise may go unnoticed due to the barriers already identified in this thesis. Educational interventions would still be required however so that once a

patient is highlighted as being at high risk, the prescriber can amend their prescription appropriately.

Finally, the SHiM tool was assessed with regard to its potential for optimising prescribing in older patients and preventing ADEs. Designed purely as a medications reconciliation tool, Chapter 7 showed that it undoubtedly optimises this process and elicits a more accurate medication list than that obtained by the attending physician. However the findings suggest it has little value for preventing ADEs (Chapter 7, Table 7.3, p145). While the majority of discrepancies identified by SHiM *did* have the potential to cause harm, suggesting it does hold some value, in terms of ADE prevention tools, this research suggests that time and resources would be better spent exploring other avenues.

9.2 Future work

The research described in this thesis provides a robust platform for further research aimed at combating PIP in older patients. Future research should focus on the following areas:

(i) Investigation of the translation of the improved prescribing skills observed in Chapter 4 into actual improvements in patient outcomes and prescribing appropriateness.

(ii) Implementation of the FI threshold system in a clinical setting to determine if this results in lower PIP and ADR incidence and prevalence.

A qualitative aspect to this research would also be useful to describe how doctors perceive such an intervention.

(iii) Improving the IT infrastructure for supporting prescribing for older patients in all levels of care in Ireland. Given the progress made in this area in other countries, there is a clear need to investigate in detail the impact of IT-supported electronic prescribing for older people in Ireland.

(iv) As stated in the literature and several times throughout this thesis, educational interventions will continue to be a vital aspect of addressing PIP in older patients. Any research driven systems or procedures put in place to aid prescribers are unlikely to achieve their full potential unless those prescribers have the fundamental skills required to make decisions with regards to older patients' pharmacotherapy. The undergraduate curriculum for medical students should also be a target for future policy makers.

9.3 Conclusions

PIP and related adverse outcomes in older patients are not attributable to one easily identifiable cause. Similarly, PIP in older patients cannot be corrected with any one easily-implemented solution. Several complex factors combine to cause suboptimal prescribing, or non-prescribing, of medications in older patients. Lack of geriatric pharmacotherapy training, dissatisfaction with prescribing guidelines, working environments conducive to PIP, patient influences and poor IT infrastructure all contribute to PIP and all must be addressed thoroughly to minimise PIP and its negative consequences. Educational interventions such as that

presented in this thesis have an important role in the continuing strive for improved prescribing for older patients. Education must be consolidated by more targeted interventions such as enabling initiatives like an FI score. Given the complex aetiology of PIP in older patients, it is likely that a multi-faceted approach is required to address this problem in a systematic way. In Ireland the lack of electronic prescribing systems is a clear barrier to minimising PIP in older patients. There is therefore, an urgent need to drastically improve the IT infrastructure in this country. Particularly in light of the rapidly growing population of older people with complex multi-morbidity and associated polypharmacy.

10. References

1. OECD (2015), Life expectancy at birth (indicator). doi: 10.1787/27e0fc9d-en (Accessed on 18 November 2015)

2. OECD (2015), Life expectancy at 65 (indicator). doi: 10.1787/0e9a3f00-en (Accessed on 18 November 2015)

3. OECD (2015), Elderly population (indicator). doi: 10.1787/8d805ea1-en (Accessed on 18 November 2015)

4. OECD (2015), Population (indicator). doi: 10.1787/d434f82b-en (Accessed on 18 November 2015)

5. Rahmner PB, Gustafsson LL, Holmstrom I, Rosenqvist U, Tomson G. Whose job is it anyway? Swedish general practitioners' perception of their responsibility for the patient's drug list. Annals of Family Medicine. 8. United States2010. p. 40-6.

6. Wetzels R, Geest TA, Wensing M, Ferreira PL, Grol R, Baker R. GPs' views on involvement of older patients: an European qualitative study. Patient Education and Counseling. 2004;53(2):183-8.

7. OECD (2015), Health spending (indicator). doi: 10.1787/8643de7e-en (Accessed on 18 November 2015)

8. OECD (2015), Hospital beds (indicator). doi: 10.1787/0191328e-en (Accessed on 18 November 2015)

9. OECD (2015), "Long-term care resources and utilisation", *OECD HealthStatistics* (database). DOI: http://dx.doi.org/10.1787/data-00543-en (Accessed on 18 November 2015)

10. OECD (2015), *Health at a Glance 2015: OECD Indicators*, OECD Publishing,Paris. DOI: http://dx.doi.org/10.1787/health_glance-2015-en

11. Gallagher P, Lang PO, Cherubini A, Topinkova E, Cruz-Jentoft A, Montero Errasquin B, et al. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. European journal of clinical pharmacology. 2011;67(11):1175-88.

12. Ryan C, O'Mahony D, Kennedy J, Weedle P, Cottrell E, Heffernan M, et al. Potentially inappropriate prescribing in older residents in Irish nursing homes. Age Ageing. 2013;42(1):116-20.

13. Ryan C, O'Mahony D, Kennedy J, Weedle P, Byrne S. Potentially inappropriate prescribing in an Irish elderly population in primary care. British journal of clinical pharmacology. 68. England2009. p. 936-47.

14. O'Sullivan D, O'Mahony D, O'Connor MN, Gallagher P, Cullinan S, O'Sullivan R, et al. The impact of a structured pharmacist intervention on the appropriateness of prescribing in older hospitalized patients. Drugs & aging. 2014;31(6):471-81.

15. O'Mahony D, Gallagher PF. Inappropriate prescribing in the older population: need for new criteria. Age Ageing. 37. England2008. p. 138-41.

16. Gallagher PF, O'Connor MN, O'Mahony D. Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria. Clinical pharmacology and therapeutics. 89. United States2011. p. 845-54.

17. O'Sullivan DP, O'Mahony D, Parsons C, Hughes C, Murphy K, Patterson S, et al. A prevalence study of potentially inappropriate prescribing in Irish long-term care residents. Drugs & aging. 2013;30(1):39-49.

18. Davidoff AJ, Miller GE, Sarpong EM, Yang E, Brandt N, Fick DM. Prevalence of potentially inappropriate medication use in older adults using the 2012 Beers criteria. Journal of the American Geriatric Society. 2015;63(3):486-500.

19. Hamano J, Tokuda Y. Inappropriate prescribing among elderly home care patients in Japan: prevalence and risk factors. Journal of primary care & community health. 2014;5(2):90-6.

20. Doody HK, Peterson GM, Watson D, Castelino RL. Retrospective evaluation of potentially inappropriate prescribing in hospitalized patients with renal impairment. Current medical research and opinion. 2015;31(3):525-35.

21. Howard M, Dolovich L, Kaczorowski J, Sellors C, Sellors J. Prescribing of potentially inappropriate medications to elderly people. Family practice. 2004;21(3):244-7.

22. Cassoni TC, Corona LP, Romano-Lieber NS, Secoli SR, Duarte YA, Lebrao ML. [Use of potentially inappropriate medication by the elderly in Sao Paulo, Brazil: SABE Study]. Cadernos de saude publica. 2014;30(8):1708-20.

23. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet. 370. England2007. p. 173-84.

24. Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. Archives of Internal Medicine. 171. United States2011. p. 1013-9.

25. Jano E, Aparasu RR. Healthcare outcomes associated with beers' criteria: a systematic review. The Annals of pharmacotherapy. 2007;41(3):438-47.

26. Laroche ML, Charmes JP, Nouaille Y, Picard N, Merle L. Is inappropriate medication use a major cause of adverse drug reactions in the elderly? British journal of clinical pharmacology. 2007;63(2):177-86.

27. Lau DT, Kasper JD, Potter DE, Lyles A, Bennett RG. Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. Archives of Internal Medicine. 2005;165(1):68-74.

28. Cahir C, Fahey T, Teeling M, Teljeur C, Feely J, Bennett K. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. British journal of clinical pharmacology. 2010;69(5):543-52.

29. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000;356(9237):1255-9.

30. International drug monitoring: the role of national centres. Report of a WHO meeting. World Health Organization technical report series. 1972;498:1-25.

31. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA : the Journal of the American Medical Association. 1998;279(15):1200-5.

32. Leendertse AJ, Egberts AC, Stoker LJ, van den Bemt PM. Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. Archives of Internal Medicine. 2008;168(17):1890-6.

33. Petrovic M, van der Cammen T, Onder G. Adverse drug reactions in older people: detection and prevention. Drugs & aging. 2012;29(6):453-62.

34. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. Pharmacy world & science : PWS. 2002;24(2):46-54.

35. Cherubini A, Ruggiero C, Gasperini B, Dell'Aquila G, Cupido MG, Zampi E, et al. The prevention of adverse drug reactions in older subjects. Current drug metabolism. 2011;12(7):652-7.

36. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing. 2008;37(6):673-9.

37. Onder G, Landi F, Liperoti R, Fialova D, Gambassi G, Bernabei R. Impact of inappropriate drug use among hospitalized older adults. European journal of clinical pharmacology. 2005;61(5-6):453-9.

38. O'Connor MN, Gallagher P, Byrne S, O'Mahony D. Adverse drug reactions in older patients during hospitalisation: are they predictable? Age Ageing. 2012;41(6):771-6.

39. Chang CM, Liu PY, Yang YH, Yang YC, Wu CF, Lu FH. Use of the Beers criteria to predict adverse drug reactions among first-visit elderly outpatients. Pharmacotherapy. 2005;25(6):831-8.

40. Budnitz DS, Shehab N, Kegler SR, Richards CL. Medication use leading to emergency department visits for adverse drug events in older adults. Annals of internal medicine. 2007;147(11):755-65.

41. Lund BC, Carnahan RM, Egge JA, Chrischilles EA, Kaboli PJ. Inappropriate prescribing predicts adverse drug events in older adults. The Annals of pharmacotherapy. 2010;44(6):957-63.

42. Hanlon JT, Schmader KE. What types of inappropriate prescribing predict adverse drug reactions in older adults? The Annals of pharmacotherapy. 2010;44(6):1110-1.

43. Alexopoulou A, Dourakis SP, Mantzoukis D, Pitsariotis T, Kandyli A, Deutsch M, et al. Adverse drug reactions as a cause of hospital admissions: a 6-month experience in a single center in Greece. European journal of internal medicine. 2008;19(7):505-10.

44. Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: inappropriate prescription is a leading cause. Drugs & aging. 2005;22(9):767-77.

45. Routledge PA, O'Mahony MS, Woodhouse KW. Adverse drug reactions in elderly patients. British journal of clinical pharmacology. 2004;57(2):121-6.

46. Hamilton HJ, Gallagher PF, O'Mahony D. Inappropriate prescribing and adverse drug events in older people. BioMed Central Geriatrics. 9. England2009. p. 5.

47. Hanlon JT, Schmader KE, Ruby CM, Weinberger M. Suboptimal prescribing in older inpatients and outpatients. Journal of the American Geriatric Society. 2001;49(2):200-9.

48. Fialova D, Topinkova E, Gambassi G, Finne-Soveri H, Jonsson PV, Carpenter I, et al. Potentially inappropriate medication use among elderly home care patients in Europe. JAMA : the journal of the American Medical Association. 2005;293(11):1348-58.

49. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR, Pirmohamed M. Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. PloS one. 2009;4(2):e4439.

50. Davies EC, Green CF, Mottram DR, Pirmohamed M. Adverse drug reactions in hospitals: a narrative review. Current drug safety. 2007;2(1):79-87.

51. Ahern F, Sahm LJ, Lynch D, McCarthy S. Determining the frequency and preventability of adverse drug reaction-related admissions to an Irish University Hospital: a cross-sectional study. Emergency medicine journal : EMJ. 2014;31(1):24-9.

52. O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. Drugs & aging. 29. New Zealand2012. p. 437-52.

53. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. British journal of clinical pharmacology. 2004;57(1):6-14.

54. Cusack B, Kelly J, O'Malley K, Noel J, Lavan J, Horgan J. Digoxin in the elderly: pharmacokinetic consequences of old age. Clinical pharmacology and therapeutics. 1979;25(6):772-6.

55. Cusack BJ. Pharmacokinetics in older persons. The American journal of geriatric pharmacotherapy. 2004;2(4):274-302.

56. Kelly JG, O'Malley K. Clinical pharmacokinetics of the newer ACE inhibitors. A review. Clinical pharmacokinetics. 1990;19(3):177-96.

57. Burnier M, Biollaz J. Pharmacokinetic optimisation of angiotensin converting enzyme (ACE) inhibitor therapy. Clinical pharmacokinetics. 1992;22(5):375-84.

58. Gregory C, McKenna P. Pharmacological management of schizophrenia in older patients. Drugs & aging. 1994;5(4):254-62.

59. Maixner SM, Mellow AM, Tandon R. The efficacy, safety, and tolerability of antipsychotics in the elderly. The Journal of clinical psychiatry. 1999;60 Suppl 8:29-41.

60. Kruse WH. Problems and pitfalls in the use of benzodiazepines in the elderly. Drug safety : an international journal of medical toxicology and drug experience. 1990;5(5):328-44.

61. Reidenberg MM, Levy M, Warner H, Coutinho CB, Schwartz MA, Yu G, et al. Relationship between diazepam dose, plasma level, age, and central nervous system depression. Clinical pharmacology and therapeutics. 1978;23(4):371-4.

62. Swift CG, Ewen JM, Clarke P, Stevenson IH. Responsiveness to oral diazepam in the elderly: relationship to total and free plasma concentrations. British journal of clinical pharmacology. 1985;20(2):111-8.

63. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Archives of Internal Medicine. 1991;151(9):1825-32.

64. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Archives of Internal Medicine. 1997;157(14):1531-6.

65. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Archives of Internal Medicine. 2003;163(22):2716-24.

66. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. Journal of the American Geriatric Society. 2012;60(4):616-31.

67. Pitkala KH, Strandberg TE, Tilvis RS. Inappropriate drug prescribing in home-dwelling, elderly patients: a population-based survey. Archives of Internal Medicine. 2002;162(15):1707-12.

68. van der Hooft CS, Jong GW, Dieleman JP, Verhamme KM, van der Cammen TJ, Stricker BH, et al. Inappropriate drug prescribing in older adults: the updated 2002 Beers criteria--a population-based cohort study. British journal of clinical pharmacology. 2005;60(2):137-44.

69. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. International Journal of Clinical Pharmacology and Therapeutics. 2008;46(2):72-83.

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

71. Ryan C, O'Mahony D, Byrne S. Application of STOPP and START criteria: interrater reliability among pharmacists. The Annals of pharmacotherapy. 2009;43(7):1239-44.

72. Gallagher P, Baeyens JP, Topinkova E, Madlova P, Cherubini A, Gasperini B, et al. Inter-rater reliability of STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. Age Ageing. 2009;38(5):603-6.

73. Liu CL, Peng LN, Chen YT, Lin MH, Liu LK, Chen LK. Potentially inappropriate prescribing (IP) for elderly medical inpatients in Taiwan: a hospital-based study. Archives of Gerontology and Geriatrics. 2012;55(1):148-51.

74. Naugler CT, Brymer C, Stolee P, Arcese ZA. Development and validation of an improving prescribing in the elderly tool. The Canadian journal of clinical pharmacology = Journal canadien de pharmacologie clinique. 2000;7(2):103-7.

75. Cantrill JA, Sibbald B, Buetow S. Indicators of the appropriateness of long-term prescribing in general practice in the United Kingdom: consensus development, face and content validity, feasibility, and reliability. Quality in health care : QHC. 1998;7(3):130-5.

76. Zhan C, Sangl J, Bierman AS, Miller MR, Friedman B, Wickizer SW, et al. Potentially inappropriate medication use in the community-dwelling elderly: findings from the 1996 Medical Expenditure Panel Survey. JAMA : the journal of the American Medical Association. 2001;286(22):2823-9.

77. Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: a French consensus panel list. European journal of clinical pharmacology. 2007;63(8):725-31.

78. Basger BJ, Chen TF, Moles RJ. Inappropriate medication use and prescribing indicators in elderly Australians: development of a prescribing indicators tool. Drugs & aging. 2008;25(9):777-93.

79. Rognstad S, Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J. The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study. Scandanavian Journal of Primary Health Care. 2009;27(3):153-9.

80. Holt S, Schmiedl S, Thuermann PA. Potentially Inappropriate Medications in the Elderly: The PRISCUS List. Deutsches Arzteblatt international. 2010;107(31-32):543-U39.

81. Winit-Watjana W, Sakulrat P, Kespichayawattana J. Criteria for high-risk medication use in Thai older patients. Archives of Gerontology and Geriatrics. 2008;47(1):35-51.

82. Rancourt C, Moisan J, Baillargeon L, Verreault R, Laurin D, Gregoire JP. Potentially inappropriate prescriptions for older patients in long-term care. BioMed Central Geriatrics. 2004;4:9.

83. Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, et al. A method for assessing drug therapy appropriateness. Journal of clinical epidemiology. 1992;45(10):1045-51.

84. Fitzgerald LS, Hanlon JT, Shelton PS, Landsman PB, Schmader KE, Pulliam CC, et al. Reliability of a modified medication appropriateness index in ambulatory older persons. The Annals of pharmacotherapy. 1997;31(5):543-8.

85. Hanlon JT, Artz MB, Pieper CF, Lindblad CI, Sloane RJ, Ruby CM, et al. Inappropriate medication use among frail elderly inpatients. The Annals of pharmacotherapy. 2004;38(1):9-14.

86. Hajjar ER, Hanlon JT, Sloane RJ, Lindblad CI, Pieper CF, Ruby CM, et al. Unnecessary drug use in frail older people at hospital discharge. Journal of the American Geriatric Society. 2005;53(9):1518-23.

87. Lipton HL, Bird JA. The impact of clinical pharmacists' consultations on geriatric patients' compliance and medical care use: a randomized controlled trial. The Gerontologist. 1994;34(3):307-15.

88. Spinewine A, Fialova D, Byrne S. The role of the pharmacist in optimizing pharmacotherapy in older people. Drugs & aging. 2012;29(6):495-510.

89. Crotty M, Halbert J, Rowett D, Giles L, Birks R, Williams H, et al. An outreach geriatric medication advisory service in residential aged care: a randomised controlled trial of case conferencing. Age Ageing. 2004;33(6):612-7.

90. Schmader KE, Hanlon JT, Pieper CF, Sloane R, Ruby CM, Twersky J, et al. Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. The American journal of medicine. 2004;116(6):394-401.

91. Strandberg TE, Pitkala KH. Frailty in elderly people. Lancet. 2007;369(9570):1328-9.

92. Strandberg TE, Pitkala KH, Berglind S, Nieminen MS, Tilvis RS. Multifactorial intervention to prevent recurrent cardiovascular events in patients 75 years or older: the Drugs and Evidence-Based Medicine in the

Elderly (DEBATE) study: a randomized, controlled trial. American Heart Journal. 2006;152(3):585-92.

93. Saltvedt I, Spigset O, Ruths S, Fayers P, Kaasa S, Sletvold O. Patterns of drug prescription in a geriatric evaluation and management unit as compared with the general medical wards: a randomised study. European journal of clinical pharmacology. 2005;61(12):921-8.

94. Deschodt M, Devriendt E, Sabbe M, Knockaert D, Deboutte P, Boonen S, et al. Characteristics of older adults admitted to the emergency department (ED) and their risk factors for ED readmission based on comprehensive geriatric assessment: a prospective cohort study. BioMed Central Geriatrics. 2015;15(1):1-10.

95. Spinewine A, Dhillon S, Mallet L, Tulkens PM, Wilmotte L, Swine C. Implementation of ward-based clinical pharmacy services in Belgium--description of the impact on a geriatric unit. The Annals of pharmacotherapy. 2006;40(4):720-8.

96. Spinewine A, Swine C, Dhillon S, Lambert P, Nachega JB, Wilmotte L, et al. Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. Journal of the American Geriatric Society. 2007;55(5):658-65.

97. Castelino RL, Bajorek BV, Chen TF. Targeting suboptimal prescribing in the elderly: a review of the impact of pharmacy services. The Annals of pharmacotherapy. 2009;43(6):1096-106.

98. Hanlon JT, Weinberger M, Samsa GP, Schmader KE, Uttech KM, Lewis IK, et al. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. The American journal of medicine. 1996;100(4):428-37.

99. Lowe CJ, Raynor DK, Purvis J, Farrin A, Hudson J. Effects of a medicine review and education programme for older people in general practice. British journal of clinical pharmacology. 2000;50(2):172-5.

100. Sellors J, Kaczorowski J, Sellors C, Dolovich L, Woodward C, Willan A, et al. A randomized controlled trial of a pharmacist consultation program for family physicians and their elderly patients. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2003;169(1):17-22.

101. Crotty M, Rowett D, Spurling L, Giles LC, Phillips PA. Does the addition of a pharmacist transition coordinator improve evidence-based medication management and health outcomes in older adults moving from the hospital to a long-term care facility? Results of a randomized,

controlled trial. The American journal of geriatric pharmacotherapy. 2004;2(4):257-64.

102. O'Sullivan D. Pharmacotherapy Optimization in Older Patients by a Structured Clinical Pharmacist Assessment and Interventions: University College Cork; 2013.

103. Loganathan M, Singh S, Franklin BD, Bottle A, Majeed A. Interventions to optimise prescribing in care homes: systematic review. Age Ageing. 2011;40(2):150-62.

104. Alldred DP, Raynor DK, Hughes C, Barber N, Chen TF, Spoor P. Interventions to optimise prescribing for older people in care homes. Cochrane database of systematic reviews (Online). 2013;2:Cd009095.

105. Gallagher P, O'Mahony D. Inappropriate prescribing in older people. Reviews in Clinical Gerontology. 2008;18(01):65-76.

106. Lutters M, Harbarth S, Janssens JP, Freudiger H, Herrmann F, Michel JP, et al. Effect of a comprehensive, multidisciplinary, educational program on the use of antibiotics in a geriatric university hospital. Journal of the American Geriatric Society. 2004;52(1):112-6.

107. Pimlott NJ, Hux JE, Wilson LM, Kahan M, Li C, Rosser WW. Educating physicians to reduce benzodiazepine use by elderly patients: a randomized controlled trial. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2003;168(7):835-9.

108. Stein CM, Griffin MR, Taylor JA, Pichert JW, Brandt KD, Ray WA. Educational program for nursing home physicians and staff to reduce use of non-steroidal anti-inflammatory drugs among nursing home residents: a randomized controlled trial. Medical Care. 2001;39(5):436-45.

109. Avorn J, Soumerai SB, Everitt DE, Ross-Degnan D, Beers MH, Sherman D, et al. A randomized trial of a program to reduce the use of psychoactive drugs in nursing homes. The New England journal of medicine. 1992;327(3):168-73.

110. Ray WA, Taylor JA, Meador KG, Lichtenstein MJ, Griffin MR, Fought R, et al. Reducing antipsychotic drug use in nursing homes. A controlled trial of provider education. Archives of Internal Medicine. 1993;153(6):713-21.

111. Rovner BW, Steele CD, Shmuely Y, Folstein MF. A randomized trial of dementia care in nursing homes. Journal of the American Geriatric Society. 1996;44(1):7-13.

112. Meador KG, Taylor JA, Thapa PB, Fought RL, Ray WA. Predictors of antipsychotic withdrawal or dose reduction in a randomized controlled trial

of provider education. Journal of the American Geriatric Society. 1997;45(2):207-10.

113. Roberts MS, Stokes JA, King MA, Lynne TA, Purdie DM, Glasziou PP, et al. Outcomes of a randomized controlled trial of a clinical pharmacy intervention in 52 nursing homes. British journal of clinical pharmacology. 2001;51(3):257-65.

114. Fossey J, Ballard C, Juszczak E, James I, Alder N, Jacoby R, et al. Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. British Medical Journal. 2006;332(7544):756-61.

115. Monette J, Miller MA, Monette M, Laurier C, Boivin JF, Sourial N, et al. Effect of an educational intervention on optimizing antibiotic prescribing in long-term care facilities. Journal of the American Geriatric Society. 2007;55(8):1231-5.

116. Wessell AM, Nietert PJ, Jenkins RG, Nemeth LS, Ornstein SM. Inappropriate medication use in the elderly: results from a quality improvement project in 99 primary care practices. The American journal of geriatric pharmacotherapy. 2008;6(1):21-7.

117. Eide E, Schjott J. Assessing the effects of an intervention by a pharmacist on prescribing and administration of hypnotics in nursing homes. Pharmacy world & science : PWS. 2001;23(6):227-31.

118. Almarsdóttir AB, Cullinan S, Masdottir BB, Byrne S. Pharmacist expertise in designing a decision support tool for optimization of drug therapy in older persons. Research in Social and Administrative Pharmacy.10(5):e38-e9.

119. Tamblyn R, Huang A, Perreault R, Jacques A, Roy D, Hanley J, et al. The medical office of the 21st century (MOXXI): effectiveness of computerized decision-making support in reducing inappropriate prescribing in primary care. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2003;169(6):549-56.

120. Peterson JF, Kuperman GJ, Shek C, Patel M, Avorn J, Bates DW. Guided prescription of psychotropic medications for geriatric inpatients. Archives of Internal Medicine. 2005;165(7):802-7.

121. Gurwitz JH, Field TS, Rochon P, Judge J, Harrold LR, Bell CM, et al. Effect of computerized provider order entry with clinical decision support on adverse drug events in the long-term care setting. Journal of the American Geriatric Society. 2008;56(12):2225-33.

122. Beers MH, Munekata M, Storrie M. The accuracy of medication histories in the hospital medical records of elderly persons. Journal of the American Geriatric Society. 1990;38(11):1183-7.

123. Field TS, Rochon P, Lee M, Gavendo L, Baril JL, Gurwitz JH. Computerized clinical decision support during medication ordering for long-term care residents with renal insufficiency. Journal of the American Medical Informatics Association : JAMIA. 2009;16(4):480-5.

124. Griffiths F, Lindenmeyer A, Powell J, Lowe P, Thorogood M. Why are health care interventions delivered over the internet? A systematic review of the published literature. Journal of medical Internet research. 2006;8(2):e10.

125. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. British Medical Journal. 2000;321(7262):694-6.

126. Christensen H, Griffiths KM, Jorm AF. Delivering interventions for depression by using the internet: randomised controlled trial. British Medical Journal. 2004;328(7434):265.

127. Andersson G, Kaldo V. Internet-based cognitive behavioral therapy for tinnitus. Journal of clinical psychology. 2004;60(2):171-8.

128. Strom L, Pettersson R, Andersson G. A controlled trial of self-help treatment of recurrent headache conducted via the Internet. Journal of consulting and clinical psychology. 2000;68(4):722-7.

129. Brennan PF, Moore SM. Networks for home care support: the ComputerLink project. Caring : National Association for Home Care magazine. 1994;13(8):64-6, 8-70.

130. Johnson KB, Ravert RD, Everton A. Hopkins Teen Central: Assessment of an internet-based support system for children with cystic fibrosis. Pediatrics. 2001;107(2):E24.

131. Delgado DH, Costigan J, Wu R, Ross HJ. An interactive Internet site for the management of patients with congestive heart failure. The Canadian journal of cardiology. 2003;19(12):1381-5.

132. Dunham PJ, Hurshman A, Litwin E, Gusella J, Ellsworth C, Dodd PW. Computer-mediated social support: single young mothers as a model system. American journal of community psychology. 1998;26(2):281-306.

133. Gray JE, Safran C, Davis RB, Pompilio-Weitzner G, Stewart JE, Zaccagnini L, et al. Baby CareLink: using the internet and telemedicine to improve care for high-risk infants. Pediatrics. 2000;106(6):1318-24.

134. Ritterband LM, Cox DJ, Walker LS, Kovatchev B, McKnight L, Patel K, et al. An Internet intervention as adjunctive therapy for pediatric encopresis. Journal of consulting and clinical psychology. 2003;71(5):910-7.

135. Verheijden M, Bakx JC, Akkermans R, van den Hoogen H, Godwin NM, Rosser W, et al. Web-based targeted nutrition counselling and social support for patients at increased cardiovascular risk in general practice: randomized controlled trial. Journal of medical Internet research. 2004;6(4):e44.

136. Winzelberg AJ, Taylor CB, Sharpe T, Eldredge KL, Dev P, Constantinou PS. Evaluation of a computer-mediated eating disorder intervention program. The International journal of eating disorders. 1998;24(4):339-49.

137. Zabinski MF, Pung MA, Wilfley DE, Eppstein DL, Winzelberg AJ, Celio A, et al. Reducing risk factors for eating disorders: targeting at-risk women with a computerized psychoeducational program. The International journal of eating disorders. 2001;29(4):401-8.

138. Designing theoretically-informed implementation interventions. Implementation science : IS. 2006;1:4.

139. Baker R, Camosso-Stefinovic J, Gillies C, Shaw EJ, Cheater F, Flottorp S, et al. Tailored interventions to overcome identified barriers to change: effects on professional practice and health care outcomes. Cochrane database of systematic reviews (Online). 2010(3):Cd005470.

140. van Bokhoven MA, Kok G, van der Weijden T. Designing a quality improvement intervention: a systematic approach. Quality and Safety in Health Care. 2003;12(3):215-20.

141. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. Health education & behavior : the official publication of the Society for Public Health Education. 1998;25(5):545-63.

142. Kok G, Schaalma H, Ruiter RA, van Empelen P, Brug J. Intervention mapping: protocol for applying health psychology theory to prevention programmes. Journal of health psychology. 2004;9(1):85-98.

143. Bowman C, Luck J, Gale RC, Smith N, York LS, Asch S. A Qualitative Evaluation of Web-Based Cancer Care Quality Improvement Toolkit Use in the Veterans Health Administration. Quality management in health care. 2015;24(3):147-61.

144. Eslamian J, Moeini M, Soleimani M. Challenges in nursing continuing education: A qualitative study. Iranian journal of nursing and midwifery research. 2015;20(3):378-86.

145. Lammers HA, van Wijnhoven R, Teunissen TA, Harmsen S, Lagro-Janssen AL. Why do men suffering from LUTS seek primary medical care? A qualitative study. Journal of evaluation in clinical practice. 2015.

146. Sale JE, Gignac M, Hawker G. How "bad" does the pain have to be? A qualitative study examining adherence to pain medication in older adults with osteoarthritis. Arthritis and rheumatism. 2006;55(2):272-8.

147. Sharma B, Ramani KV, Mavalankar D, Kanguru L, Hussein J. Using 'appreciative inquiry' in India to improve infection control practices in maternity care: a qualitative study. Global health action. 2015;8:26693.

148. Stenner R, Swinkels A, Mitchell T, Palmer S. Exercise prescription for patients with non-specific chronic low back pain: a qualitative exploration of decision making in physiotherapy practice. Physiotherapy. 2015.

149. Tonkin-Crine S, Santer M, Leydon GM, Murtagh FE, Farrington K, Caskey F, et al. GPs' views on managing advanced chronic kidney disease in primary care: a qualitative study. The British journal of general practice : the journal of the Royal College of General Practitioners. 2015;65(636):e469-77.

150. Zegwaard MI, Aartsen MJ, Grypdonck MH, Cuijpers P. Mental health nurses' support to caregivers of older adults with severe mental illness: a qualitative study. BioMed Central Nursing. 2015;14:37.

151. Al-Busaidi ZQ. Qualitative research and its uses in health care. Sultan Qaboos University medical journal. 2008;8(1):11-9.

152. Poses RM, Isen AM. Qualitative research in medicine and health care: questions and controversy. Journal of general internal medicine. 1998;13(1):32-8.

153. Pope C, van Royen P, Baker R. Qualitative methods in research on healthcare quality. Quality and Safety in Health Care. 2002;11(2):148-52.

154. Murphy E, Dingwall R, Greatbatch D, Parker S, Watson P. Qualitative research methods in health technology assessment: a review of the literature. Health technology assessment (Winchester, England). 1998;2(16):iii-ix, 1-274.

155. Pope C, Mays N. Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. British Medical Journal. 1995;311(6996):42-5.

156. Cullinan S, O'Mahony D, Fleming A, Byrne S. A Meta-Synthesis of Potentially Inappropriate Prescribing in Older Patients. Drugs & aging. 2014;31(8):631-8.

157. Damestoy N, Collin J, Lalande R. Prescribing psychotropic medication for elderly patients: some physicians' perspectives. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 1999;161(2):143-5.

158. Cook JM, Marshall R, Masci C, Coyne JC. Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study. Journal of general internal medicine. 2007;22(3):303-7.

159. Agarwal G, Nair K, Cosby J, Dolovich L, Levine M, Kaczorowski J, et al. GPs' approach to insulin prescribing in older patients: a qualitative study. British Journal of General Practice. 2008;58(553):569-75.

160. Wood-Mitchell A, James IA, Waterworth A, Swann A, Ballard C. Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study. Age and Ageing. 2008;37(5):547-52.

161. Dickinson R, Knapp P, House AO, Dimri V, Zermansky A, Petty D, et al. Long-term prescribing of antidepressants in the older population: a qualitative study. British Journal of General Practice. 2010;60(573):257-9.

162. Spitz A, Moore AA, Papaleontiou M, Granieri E, Turner BJ, Reid MC. Primary care providers' perspective on prescribing opioids to older adults with chronic non-cancer pain: a qualitative study. BioMed Central Geriatrics. 11. England2011. p. 35.

163. Dunn RL, Harrison D, Ripley TL. The beers criteria as an outpatient screening tool for potentially inappropriate medications. Consultant Pharmacist. 26. United States2011. p. 754-63.

164. Spiker EC, Emptage RE, Giannamore MR, Pedersen CA. Potential adverse drug events in an indigent and homeless geriatric population. The Annals of pharmacotherapy. 2001;35(10):1166-72.

165. Chrischilles EA, VanGilder R, Wright K, Kelly M, Wallace RB. Inappropriate medication use as a risk factor for self-reported adverse drug. Journal of the American Geriatric Society. 2009;57(6):1000-6.

166. Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: inappropriate. Drugs & aging. 2005;22(9):767-77.

167. Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, et al. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. Social science & medicine (1982). 56. England2003. p. 671-84.

168. Campbell R, Pound P, Morgan M, Daker-White G, Britten N, Pill R, et al. Evaluating meta-ethnography: systematic analysis and synthesis of qualitative research. Health technology assessment (Winchester, England). 2011;15(43):1-164.

169. Atkins S, Lewin S, Smith H, Engel M, Fretheim A, Volmink J. Conducting a meta-ethnography of qualitative literature: lessons learnt. BMC medical research methodology. 8. England2008. p. 21.

170. Malpass A, Shaw A, Sharp D, Walter F, Feder G, Ridd M, et al. "Medication career" or "moral career"? The two sides of managing antidepressants: a meta-ethnography of patients' experience of antidepressants. Social science & medicine (1982). 68. England2009. p. 154-68.

171. Noblit GW, Hare RD. Meta-Ethnography: synthesising qualitative studies. London:Sage. 1988.

172. Pound P, Britten N, Morgan M, Yardley L, Pope C, Daker-White G, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. Social Science & Medicine. 2005;61(1):133-55.

173. Britten N, Campbell R, Pope C, Donovan J, Morgan M, Pill R. Using meta ethnography to synthesise qualitative research: a worked example. Journal of health services research & policy. 2002;7(4):209-15.

174. Teixeira Rodrigues A, Roque F, Falcao A, Figueiras A, Herdeiro MT. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies. International journal of antimicrobial agents. 2013;41(3):203-12.

175. Thorne S, Jensen L, Kearney MH, Noblit G, Sandelowski M. Qualitative metasynthesis: reflections on methodological orientation and. Qualitative health research. 2004;14(10):1342-65.

176. Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC medical research methodology. 2012;12:181.

177. Spinewine A, Swine C, Dhillon S, Franklin BD, Tulkens PM, Wilmotte L, et al. Appropriateness of use of medicines in elderly inpatients: qualitative study. British Medical Journal. 331. England2005. p. 935.

178. Salzman C. The APA Task Force report on benzodiazepine dependence, toxicity, and abuse. The American journal of psychiatry. 1991;148(2):151-2.

179. Consensus conference. Drugs and insomnia. The use of medications to promote. JAMA : the journal of the American Medical Association. 1984;251(18):2410-4.

180. Spinewine A, Swine C, Dhillon S, Franklin BD, Tulkens PM, Wilmotte L, et al. Appropriateness of use of medicines in elderly inpatients: Qualitative study. British Medical Journal. 2005;331(7522):935-8.

181. Murie J, Allen J, Simmonds R, de Wet C. Glad you brought it up: a patient-centred programme to reduce proton-pump inhibitor prescribing in general medical practice. Quality in Primary Care. 2012;20(2):141-8.

182. Hamzat H, Sun H, Ford JC, Macleod J, Soiza RL, Mangoni AA. Inappropriate prescribing of proton pump inhibitors in older patients: effects of an educational strategy. Drugs & aging. 2012;29(8):681-90.

183. Chan AH, Garratt E, Lawrence B, Turnbull N, Pratapsingh P, Black PN. Effect of education on the recording of medicines on admission to hospital. Journal of general internal medicine. 2010;25(6):537-42.

184. Thornley SM, Carmichael JM, Bryg RJ. Effect of clinical pharmacy input on physician prescribing habits in the nursing home care unit. Hospital pharmacy. 1992;27(7):616-7, 21.

185. Gordon M. Non-technical skills training to enhance patient safety. The clinical teacher. 2013;10(3):170-5.

186. Kinsella K, Wan H. An aging world: 2008. 2009.

187. Cherubini A, Corsonello A, Lattanzio F. Underprescription of beneficial medicines in older people: causes, consequences and prevention. Drugs & aging. 29. New Zealand2012. p. 463-75.

188. Steinman MA, Landefeld CS, Rosenthal GE, Berthenthal D, Sen S, Kaboli PJ. Polypharmacy and prescribing quality in older people. Journal of the American Geriatric Society. 54. United States2006. p. 1516-23.

189. Cook JM, Marshall R, Masci C, Coyne JC. Physicians' perspectives on prescribing benzodiazepines for older adults: A qualitative study. Journal of general internal medicine. 2007;22(3):303-7.

190. Dickinson R, Knapp P, Dimri V, Holmes J, House A, Petty D, et al. The long-term use of antidepressants in the older population: A qualitative study. International Journal of Pharmacy Practice. 2009;17(S2):B26.

191. Boscart VM, Fernie GR, Lee JH, Jaglal SB. Using psychological theory to inform methods to optimize the implementation of a hand hygiene intervention. Implementation science : IS. 2012;7:77.

192. Albarracin D, Gillette JC, Earl AN, Glasman LR, Durantini MR, Ho MH. A test of major assumptions about behavior change: a comprehensive look at the effects of passive and active HIV-prevention interventions since the beginning of the epidemic. Psychological bulletin. 2005;131(6):856-97.

193. Noar SM, Zimmerman RS. Health Behavior Theory and cumulative knowledge regarding health behaviors: are we moving in the right direction? Health Education Research. 2005;20(3):275-90.

194. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A. Making psychological theory useful for implementing evidence based practice: a consensus approach. Quality and Safety in Health Care. 2005;14(1):26-33.

195. Pitt VJ, O'Connor D, Green S. Referral of people with osteoarthritis to self-management programmes: barriers and enablers identified by general practitioners. Disability and rehabilitation. 2008;30(25):1938 - 46.

196. Amemori M, Michie S, Korhonen T, Murtomaa H, Kinnunen TH. Assessing implementation difficulties in tobacco use prevention and cessation counselling among dental providers. Implementation science : IS. 2011;6:50.

197. Duncan EM, Francis JJ, Johnston M, Davey P, Maxwell S, McKay GA, et al. Learning curves, taking instructions, and patient safety: using a theoretical domains framework in an interview study to investigate prescribing errors among trainee doctors. Implementation science : IS. 2012;7:86.

198. Michie S, Johnston M, Francis J, Hardeman W, Eccles M. From theory to intervention: Mapping theoretically derived behavioural determinants to behaviour change techniques. Applied Psychology-an International Review-Psychologie Appliquee-Revue Internationale. 2008;57(4):660-80.

199. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. Implementation science : IS. 2012;7:37.

200. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implementation science : IS. 2011;6:42.

201. S M, editor The behaviour change wheel, theoretical domains framework, behaviour change techniques2012; KT Terminology Meeting, Ottawa, Canada.

202. J R, J L. Qualitative Research Practice A Guide for Social Science Students and Researchers: Sage publications; 2008.

203. Dyson J, Lawton R, Jackson C, Cheater F. Does the use of a theoretical approach tell us more about hand hygiene behaviour? The barriers and levers to hand hygiene. Journal of Infection Prevention. 2011;12(1):17-24.

204. Ritchie J, Spencer L. Qualitative data analysis for applied policy research. Bryman A BR, editor. London: Routledge1994.

205. Hsieh H-F, Shannon SE. Three Approaches to Qualitative Content Analysis. Qualitative health research. 2005;15(9):1277-88.

206. Carey JW, Morgan M, Oxtoby MJ. Intercoder Agreement in Analysis of Responses to Open-Ended Interview Questions: Examples from Tuberculosis Research. Field Methods. 1996;8(3):1-5.

207. Francis JJ, Johnston M, Robertson C, Glidewell L, Entwistle V, Eccles MP, et al. What is an adequate sample size? Operationalising data saturation for theory-based interview studies. Psychology & health. 2010;25(10):1229-45.

208. Dean B, Schachter M, Vincent C, Barber N. Causes of prescribing errors in hospital inpatients: a prospective study. Lancet. 2002;359(9315):1373-8.

209. Coombes ID, Stowasser DA, Coombes JA, Mitchell C. Why do interns make prescribing errors? A qualitative study. Medical Journal of Australia. 2008;188(2):89-94.

210. Aronson JK. Balanced prescribing - principles and challenges. British journal of clinical pharmacology. 2012;74(4):566-72.

211. Aronson JK, Barnett DB, Ferner RE, Ferro A, Henderson G, Maxwell SR, et al. Poor prescribing is continual. British Medical Journal. 2006;333(7571):756.

212. Aronson JK, Henderson G, Webb DJ, Rawlins MD. A prescription for better prescribing. British Medical Journal. 2006;333(7566):459-60.

213. Davis RE, Dolan G, Thomas S, Atwell C, Mead D, Nehammer S, et al. Exploring doctor and patient views about risk communication and shared decision-making in the consultation. Health Expectations. 2003;6(3):198-207.

214. Gallagher P, Barry P, O'Mahony D. Inappropriate prescribing in the elderly. Journal of Clinical Pharmacy and Therapeutics. 32. England2007. p. 113-21.

215. Cullinan S, Fleming A, O'Mahony D, Ryan C, O'Sullivan D, Gallagher P, et al. Doctors' perspectives on the barriers to appropriate prescribing in

older hospitalized patients: A qualitative study. British journal of clinical pharmacology. 2014.

216. Coombes ID, Mitchell CA, Stowasser DA. Safe medication practice: attitudes of medical students about to begin their intern year. Medical education. 2008;42(4):427-31.

217. Garbutt JM, Highstein G, Jeffe DB, Dunagan WC, Fraser VJ. Safe medication prescribing: training and experience of medical students and housestaff at a large teaching hospital. Academic medicine : journal of the Association of American Medical Colleges. 2005;80(6):594-9.

218. Cook DA, Levinson AJ, Garside S, Dupras DM, Erwin PJ, Montori VM. Internet-based learning in the health professions: a meta-analysis. JAMA : the journal of the American Medical Association. 2008;300(10):1181-96.

219. Ryan G, Lyon P, Kumar K, Bell J, Barnet S, Shaw T. Online CME: an effective alternative to face-to-face delivery. Medical teacher. 2007;29(8):e251-7.

220. Jayakumar N, Brunckhorst O, Dasgupta P, Khan MS, Ahmed K. e-Learning in Surgical Education: A Systematic Review. Journal of surgical education. 2015.

221. Gordon M, Chandratilake M, Baker P. Improved junior paediatric prescribing skills after a short e-learning intervention: a randomised controlled trial. Archives of disease in childhood. 2011;96(12):1191-4.

222. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Annals of internal medicine. 2010;152(11):726-32.

223. Ajemigbitse AA, Omole MK, Ezike NC, Erhun WO. Assessment of the knowledge and attitudes of intern doctors to medication prescribing errors in a Nigeria tertiary hospital. Journal of basic and clinical pharmacy. 2013;5(1):7-14.

224. Pearson SA, Rolfe I, Smith T. Factors influencing prescribing: an intern's perspective. Medical education. 2002;36(8):781-7.

225. Cohen MD, Hilligoss PB. The published literature on handoffs in hospitals: deficiencies identified in an extensive review. Quality and Safety in Health Care. 2010;19(6):493-7.

226. Council NR. The Prevention and Treatment of Missing Data in Clinical Trials. Washington, DC: The National Academies Press; 2010. 162 p.

227. Chen X, Mao G, Leng SX. Frailty syndrome: an overview. Clinical interventions in aging. 2014;9:433-41.

228. Lipsitz LA. Dynamics of stability: the physiologic basis of functional health and frailty. The journals of gerontology Series A, Biological sciences and medical sciences. 2002;57(3):B115-25.

229. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in Older Adults: Evidence for a Phenotype. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2001;56(3):M146-M57.

230. Bortz WM, 2nd. The physics of frailty. Journal of the American Geriatric Society. 1993;41(9):1004-8.

231. Buigues C, Padilla-Sanchez C, Garrido JF, Navarro-Martinez R, Ruiz-Ros V, Cauli O. The relationship between depression and frailty syndrome: a systematic review. Aging & mental health. 2015;19(9):762-72.

232. White HD, Westerhout CM, Alexander KP, Roe MT, Winters KJ, Cyr DD, et al. Frailty is associated with worse outcomes in non-ST-segment elevation acute coronary syndromes: Insights from the TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medicallY manage Acute Coronary Syndromes (TRILOGY ACS) trial. European heart journal Acute cardiovascular care. 2015.

233. Sanchis J, Bonanad C, Ruiz V, Fernandez J, Garcia-Blas S, Mainar L, et al. Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome. American Heart Journal. 2014;168(5):784-91.

234. Bagshaw SM, Stelfox HT, McDermid RC, Rolfson DB, Tsuyuki RT, Baig N, et al. Association between frailty and short- and long-term outcomes among critically ill patients: a multicentre prospective cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2014;186(2):E95-102.

235. Bagshaw SM, McDermid RC. The role of frailty in outcomes from critical illness. Current opinion in critical care. 2013;19(5):496-503.

236. Faria Cde A, Lourenco RA, Ribeiro PC, Lopes CS. [Cognitive performance and frailty in older adults clients of a private health care plan]. Rev Saude Publica. 2013;47(5):923-30.

237. Johnston C, Hilmer SN, McLachlan AJ, Matthews ST, Carroll PR, Kirkpatrick CM. The impact of frailty on pharmacokinetics in older people: using gentamicin population pharmacokinetic modeling to investigate changes in renal drug clearance by glomerular filtration. European journal of clinical pharmacology. 2014;70(5):549-55.

238. Partridge JS, Harari D, Dhesi JK. Frailty in the older surgical patient: a review. Age Ageing. 2012;41(2):142-7.

239. Leng S, Chaves P, Koenig K, Walston J. Serum interleukin-6 and hemoglobin as physiological correlates in the geriatric syndrome of frailty: a pilot study. Journal of the American Geriatric Society. 2002;50(7):1268-71.

240. Leng SX, Xue QL, Tian J, Walston JD, Fried LP. Inflammation and frailty in older women. Journal of the American Geriatric Society. 2007;55(6):864-71.

241. Yao X, Li H, Leng SX. Inflammation and immune system alterations in frailty. Clinics in geriatric medicine. 2011;27(1):79-87.

242. Li H, Manwani B, Leng SX. Frailty, inflammation, and immunity. Aging and disease. 2011;2(6):466-73.

243. Walston J, Fedarko N, Yang H, Leng S, Beamer B, Espinoza S, et al. The physical and biological characterization of a frail mouse model. The journals of gerontology Series A, Biological sciences and medical sciences. 2008;63(4):391-8.

244. Collerton J, Martin-Ruiz C, Davies K, Hilkens CM, Isaacs J, Kolenda C, et al. Frailty and the role of inflammation, immunosenescence and cellular ageing in the very old: cross-sectional findings from the Newcastle 85+ Study. Mechanisms of ageing and development. 2012;133(6):456-66.

245. Walston J, McBurnie MA, Newman A, Tracy RP, Kop WJ, Hirsch CH, et al. Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities: results from the Cardiovascular Health Study. Archives of Internal Medicine. 2002;162(20):2333-41.

246. Leng SX, Tian X, Matteini A, Li H, Hughes J, Jain A, et al. IL-6-independent association of elevated serum neopterin levels with prevalent frailty in community-dwelling older adults. Age Ageing. 2011;40(4):475-81.

247. Ramanathan R, Kohli A, Ingaramo MC, Jain A, Leng SX, Punjabi NM, et al. Serum chitotriosidase, a putative marker of chronically activated macrophages, increases with normal aging. The journals of gerontology Series A, Biological sciences and medical sciences. 2013;68(10):1303-9.

248. Semba RD, Margolick JB, Leng S, Walston J, Ricks MO, Fried LP. T cell subsets and mortality in older community-dwelling women. Experimental gerontology. 2005;40(1-2):81-7.

249. Qu T, Yang H, Walston JD, Fedarko NS, Leng SX. Upregulated monocytic expression of CXC chemokine ligand 10 (CXCL-10) and its relationship with serum interleukin-6 levels in the syndrome of frailty. Cytokine. 2009;46(3):319-24.

250. Schmaltz HN, Fried LP, Xue QL, Walston J, Leng SX, Semba RD. Chronic cytomegalovirus infection and inflammation are associated with prevalent frailty in community-dwelling older women. Journal of the American Geriatric Society. 2005;53(5):747-54.

251. Visser M, Pahor M, Taaffe DR, Goodpaster BH, Simonsick EM, Newman AB, et al. Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. The journals of gerontology Series A, Biological sciences and medical sciences. 2002;57(5):M326-32.

252. Ferrucci L, Penninx BW, Volpato S, Harris TB, Bandeen-Roche K, Balfour J, et al. Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. Journal of the American Geriatric Society. 2002;50(12):1947-54.

253. Leng SX, Cappola AR, Andersen RE, Blackman MR, Koenig K, Blair M, et al. Serum levels of insulin-like growth factor-I (IGF-I) and dehydroepiandrosterone sulfate (DHEA-S), and their relationships with serum interleukin-6, in the geriatric syndrome of frailty. Aging clinical and experimental research. 2004;16(2):153-7.

254. Leng SX, Hung W, Cappola AR, Yu Q, Xue QL, Fried LP. White blood cell counts, insulin-like growth factor-1 levels, and frailty in community-dwelling older women. The journals of gerontology Series A, Biological sciences and medical sciences. 2009;64(4):499-502.

255. Liu LK, Lee WJ, Liu CL, Chen LY, Lin MH, Peng LN, et al. Age-related skeletal muscle mass loss and physical performance in Taiwan: implications to diagnostic strategy of sarcopenia in Asia. Geriatrics & gerontology international. 2013;13(4):964-71.

256. Rockwood K, Bergman H. FRAILTY: A Report from the 3(rd) Joint Workshop of IAGG/WHO/SFGG, Athens, January 2012. Canadian geriatrics journal : CGJ. 2012;15(2):31-6.

257. Puts MT, Visser M, Twisk JW, Deeg DJ, Lips P. Endocrine and inflammatory markers as predictors of frailty. Clinical endocrinology. 2005;63(4):403-11.

258. Varadhan R, Walston J, Cappola AR, Carlson MC, Wand GS, Fried LP. Higher levels and blunted diurnal variation of cortisol in frail older women. The journals of gerontology Series A, Biological sciences and medical sciences. 2008;63(2):190-5.

259. Shardell M, Hicks GE, Miller RR, Kritchevsky S, Andersen D, Bandinelli S, et al. Association of low vitamin D levels with the frailty syndrome in men and women. The journals of gerontology Series A, Biological sciences and medical sciences. 2009;64(1):69-75.

260. Blaum CS, Xue QL, Michelon E, Semba RD, Fried LP. The association between obesity and the frailty syndrome in older women: the Women's Health and Aging Studies. Journal of the American Geriatric Society. 2005;53(6):927-34.

261. Woods NF, LaCroix AZ, Gray SL, Aragaki A, Cochrane BB, Brunner RL, et al. Frailty: emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. Journal of the American Geriatric Society. 2005;53(8):1321-30.

262. Hubbard RE, Lang IA, Llewellyn DJ, Rockwood K. Frailty, body mass index, and abdominal obesity in older people. The journals of gerontology Series A, Biological sciences and medical sciences. 2010;65(4):377-81.

263. Strandberg TE, Sirola J, Pitkala KH, Tilvis RS, Strandberg AY, Stenholm S. Association of midlife obesity and cardiovascular risk with old age frailty: a 26-year follow-up of initially healthy men. International journal of obesity (2005). 2012;36(9):1153-7.

264. Theou O, Stathokostas L, Roland KP, Jakobi JM, Patterson C, Vandervoort AA, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. Journal of aging research. 2011;2011:569194.

265. Gill TM, Baker DI, Gottschalk M, Peduzzi PN, Allore H, Byers A. A program to prevent functional decline in physically frail, elderly persons who live at home. The New England journal of medicine. 2002;347(14):1068-74.

266. Fiatarone MA, O'Neill EF, Ryan ND, Clements KM, Solares GR, Nelson ME, et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. The New England journal of medicine. 1994;330(25):1769-75.

267. Forster A, Lambley R, Hardy J, Young J, Smith J, Green J, et al. Rehabilitation for older people in long-term care. Cochrane database of systematic reviews (Online). 2009(1):Cd004294.

268. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. The journals of gerontology Series A, Biological sciences and medical sciences. 2007;62(7):722-7.

269. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. Journal of the American Medical Directors Association. 2013;14(6):392-7.

270. Abellan van Kan G, Rolland Y, Bergman H, Morley JE, Kritchevsky SB, Vellas B. The I.A.N.A Task Force on frailty assessment of older people in clinical practice. The journal of nutrition, health & aging. 2008;12(1):29-37.

271. Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). BioiMed Central Geriatrics. 2010;10:57.

272. Peters LL, Boter H, Buskens E, Slaets JP. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. Journal of the American Medical Directors Association. 2012;13(6):546-51.

273. Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a standardized comprehensive geriatric assessment. Journal of the American Geriatrics Society. 2004;52(11):1929-33.

274. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. Clinics in geriatric medicine. 2011;27(1):17-26.

275. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BioMed Central Geriatrics. 2008;8:24.

276. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. TheScientificWorldJournal. 2001;1:323-36.

277. Rockwood K, Hogan DB, MacKnight C. Conceptualisation and measurement of frailty in elderly people. Drugs & aging. 2000;17(4):295-302.

278. Mitnitski A, Song X, Skoog I, Broe GA, Cox JL, Grunfeld E, et al. Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. Journal of the American Geriatrics Society. 2005;53(12):2184-9.

279. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. The journals of gerontology Series A, Biological sciences and medical sciences. 2007;62(7):738-43.

280. Kulminski A, Yashin A, Arbeev K, Akushevich I, Ukraintseva S, Land K, et al. Cumulative index of health disorders as an indicator of aging-associated processes in the elderly: results from analyses of the National Long Term Care Survey. Mechanisms of ageing and development. 2007;128(3):250-8.

281. Goggins WB, Woo J, Sham A, Ho SC. Frailty index as a measure of biological age in a Chinese population. The journals of gerontology Series A, Biological sciences and medical sciences. 2005;60(8):1046-51.

282. Woo J, Goggins W, Sham A, Ho SC. Social determinants of frailty. Gerontology. 2005;51(6):402-8.

283. Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: different instruments for different purposes. Age Ageing. 2014;43(1):10-2.

284. Bergman H, Ferrucci L, Guralnik J, Hogan DB, Hummel S, Karunananthan S, et al. Frailty: An Emerging Research and Clinical Paradigm—Issues and Controversies. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2007;62(7):731-7.

285. Fisher AL. Just What Defines Frailty? Journal of the American Geriatrics Society. 2005;53(12):2229-30.

286. Andrew MK, Fisk JD, Rockwood K. Social vulnerability and prefrontal cortical function in elderly people: a report from the Canadian Study of Health and Aging. International psychogeriatrics / IPA. 2011;23(3):450-8.

287. O'Sullivan D, O'Mahony D, O'Connor MN, Gallagher P, Cullinan S, O'Sullivan R, Gallagher J, Eustace J, Byrne S. The impact of a structured pharmacist intervention on the appropriateness of prescribing in older hospitalized patients. Drugs Aging. 2014;(6):471-81

288. Gupta SK, Nayak RP, Shivaranjani R, Vidyarthi SK. A questionnaire study on the knowledge, attitude, and the practice of pharmacovigilance among the healthcare professionals in a teaching hospital in South India. Perspectives in clinical research. 2015;6(1):45-52.

289. Forsetlund L, Eike MC, Gjerberg E, Vist GE. Effect of interventions to reduce potentially inappropriate use of drugs in nursing homes: a systematic review of randomised controlled trials. BioMed Central Geriatrics. 2011;11:16.

290. Drubbel I, de Wit NJ, Bleijenberg N, Eijkemans RJ, Schuurmans MJ, Numans ME. Prediction of adverse health outcomes in older people using a frailty index based on routine primary care data. The journals of gerontology Series A, Biological sciences and medical sciences. 2013;68(3):301-8.

291. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. Age Ageing. 2015;44(1):148-52.

292. Hubbard RE, Peel NM, Samanta M, Gray LC, Fries BE, Mitnitski A, et al. Derivation of a frailty index from the interRAI acute care instrument. BioMed Central Geriatrics. 2015;15:27.

293. Andersen SE, Pedersen AB, Bach KF. Medication history on internal medicine wards: assessment of extra information collected from second drug interviews and GP lists. Pharmacoepidemiology and Drug Safety. 2003;12(6):491-8.

294. Atkin PA, Stringer RS, Duffy JB, Elion C, Ferraris CS, Misrachi SR, et al. The influence of information provided by patients on the accuracy of medication records. The Medical journal of Australia. 1998;169(2):85-8.

295. Institute of Medicine Committee on Quality of Health Care in A. In: Kohn LT, Corrigan JM, Donaldson MS, editors. To Err is Human: Building a Safer Health System. Washington (DC): National Academies Press (US)

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296. Tam VC, Knowles SR, Cornish PL, Fine N, Marchesano R, Etchells EE. Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2005;173(5):510-5.

297. Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA : the journal of the American Medical Association. 1997;277(4):307-11.

298. Cornish PL, Knowles SR, Marchesano R, Tam V, Shadowitz S, Juurlink DN, et al. Unintended medication discrepancies at the time of hospital admission. Arch Intern Med. 2005;165(4):424-9.

299. Gleason KM, Groszek JM, Sullivan C, Rooney D, Barnard C, Noskin GA. Reconciliation of discrepancies in medication histories and admission orders of newly hospitalized patients. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2004;61(16):1689-95.

300. Drenth-van Maanen AC, Spee J, van Hensbergen L, Jansen PA, Egberts TC, van Marum RJ. Structured history taking of medication use reveals iatrogenic harm due to discrepancies in medication histories in hospital and pharmacy records. Journal of the American Geriatrics Society. 2011;59(10):1976-7.

301. Lau HS, Florax C, Porsius AJ, De Boer A. The completeness of medication histories in hospital medical records of patients admitted to general internal medicine wards. British journal of clinical pharmacology. 2000;49(6):597-603.

302. Unroe KT, Pfeiffenberger T, Riegelhaupt S, Jastrzembski J, Lokhnygina Y, Colon-Emeric C. Inpatient medication reconciliation at admission and discharge: A retrospective cohort study of age and other risk factors for medication discrepancies. The American journal of geriatric pharmacotherapy. 2010;8(2):115-26.

303. Steurbaut S, Leemans L, Leysen T, De Baere E, Cornu P, Mets T, et al. Medication history reconciliation by clinical pharmacists in elderly inpatients admitted from home or a nursing home. The Annals of pharmacotherapy. 2010;44(10):1596-603.

304. Rozich JD, Howard RJ, Justeson JM, Macken PD, Lindsay ME, Resar RK. Standardization as a mechanism to improve safety in health care. Joint Commission journal on quality and safety. 2004;30(1):5-14.

305. Michels RD, Meisel SB. Program using pharmacy technicians to obtain medication histories. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2003;60(19):1982-6.

306. Rodehaver C, Fearing D. Medication reconciliation in acute care: ensuring an accurate drug regimen on admission and discharge. Joint Commission journal on quality and patient safety / Joint Commission Resources. 2005;31(7):406-13.

307. Vira T, Colquhoun M, Etchells E. Reconcilable differences: correcting medication errors at hospital admission and discharge. Quality and Safety in Health Care. 2006;15(2):122-6.

308. Boockvar KS, Blum S, Kugler A, Livote E, Mergenhagen KA, Nebeker JR, et al. Effect of admission medication reconciliation on adverse drug events from admission medication changes. Archives of Internal Medicine. 2011;171(9):860-1.

309. Pippins JR, Gandhi TK, Hamann C, Ndumele CD, Labonville SA, Diedrichsen EK, et al. Classifying and predicting errors of inpatient medication reconciliation. Journal of general internal medicine. 2008;23(9):1414-22.

310. Galvin M, Jago-Byrne MC, Fitzsimons M, Grimes T. Clinical pharmacist's contribution to medication reconciliation on admission to hospital in Ireland. International journal of clinical pharmacy. 2013;35(1):14-21.

311. Hellstrom LM, Bondesson A, Hoglund P, Eriksson T. Errors in medication history at hospital admission: prevalence and predicting factors. BioMed Central clinical pharmacology. 2012;12:9.

312. Organisation WH. Assuring Medication Accuracy at Transitions in Care. Geneva: World Health Organisation (WHO) 2007.

313. Fitzgerald RJ. Medication errors: the importance of an accurate drug history. British journal of clinical pharmacology. 2009;67(6):671-5.

314. Warholak TL, McCulloch M, Baumgart A, Smith M, Fink W, Fritz W. An exploratory comparison of medication lists at hospital admission with administrative database records. Journal of managed care pharmacy : JMCP. 2009;15(9):751-8.

315. Reeder TA, Mutnick A. Pharmacist- versus physician-obtained medication histories. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2008;65(9):857-60.

316. ActiZ GN, KNMG, KNMP, LEVV, LHV. Dutch Guideline 'Transfer of medication data'. 112-2-2008 Ref Type: Generic. 2008.

317. Henneman EA, Tessier EG, Nathanson BH, Plotkin K. An evaluation of a collaborative, safety focused, nurse-pharmacist intervention for improving the accuracy of the medication history. Journal of patient safety. 2014;10(2):88-94.

318. Prins MC, Drenth-van Maanen AC, Kok RM, Jansen PA. Use of a structured medication history to establish medication use at admission to an old age psychiatric clinic: a prospective observational study. CNS drugs. 2013;27(11):963-9.

319. De Winter S, Spriet I, Indevuyst C, Vanbrabant P, Desruelles D, Sabbe M, et al. Pharmacist- versus physician-acquired medication history: a prospective study at the emergency department. Quality and Safety in Health Care. 2010;19(5):371-5.

320. Bell HT, Steinsbekk A, Granas AG. Factors influencing prescribing of fall-risk-increasing drugs to the elderly: A qualitative study. Scandanavian Journal of Primary Health Care. 2015;33(2):107-14.

321. Magin P, Goode S, Pond D. GPs, medications and older people: A qualitative study of general practitioners' approaches to potentially inappropriate medications in older people. Australasian journal on ageing. 2015;34(2):134-9.

322. Garside R. A Comparison of methods for the Systematic Review of Qualitative Research : Two Examples Using Meta-Ethnography and Meta-Study: University of Exeter; 2008.

323. Finfgeld-Connett D. Meta-synthesis of caring in nursing. Journal of Clinical Nursing. 2008;17(2):196-204.

324. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. BMJ Open. 2014;4(12):e006544.

325. Gordon M, Darbyshire D, Baker P. Non-technical skills training to enhance patient safety: a systematic review. Medical education. 2012;46(11):1042-54.

326. Clyne B, Bradley MC, Hughes CM, Clear D, McDonnell R, Williams D, et al. Addressing potentially inappropriate prescribing in older patients: development and pilot study of an intervention in primary care (the OPTI-SCRIPT study). BioMed Central Health Services Research. 2013;13:307.

327. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ : British Medical Journal. 2008;337:a1655.

328. Clyne B, Bradley MC, Smith SM, Hughes CM, Motterlini N, Clear D, et al. Effectiveness of medicines review with web-based pharmaceutical treatment algorithms in reducing potentially inappropriate prescribing in older people in primary care: a cluster randomized trial (OPTI-SCRIPT study protocol). Trials. 2013;14:72.

329. Guchelaar HJ, Kalmeijer MD. The potential role of computerisation and information technology in improving prescribing in hospitals. Pharmacy World and Science. 2003;25(3):83-7.

330. Agrawal A. Medication errors: prevention using information technology systems. British journal of clinical pharmacology. 2009;67(6):681-6.

331. Forster AJ, Auger C, f IAI. USing information technology to improve the monitoring of outpatient prescribing. Journal of the American Medical Association Internal Medicine. 2013;173(5):382-4.

332. Porterfield A, Engelbert K, Coustasse A. Electronic prescribing: improving the efficiency and accuracy of prescribing in the ambulatory care setting. Perspectives in health information management / AHIMA, American Health Information Management Association. 2014;11:1g.

11. Appendices

11.1 Appendix I: A meta-synthesis of potentially inappropriate prescribing in older patients

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Drugs Aging (2014) 31:631–638
DOI 10.1007/s40266-014-0190-4

ORIGINAL RESEARCH ARTICLE

A Meta-Synthesis of Potentially Inappropriate Prescribing in Older Patients

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Published online: 13 June 2014
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Abstract

Background Potentially inappropriate prescribing (PIP) is commonly seen amongst the older population in all clinical settings, as indicated by several prevalence studies in several countries. Quantitative work such as this confirms that this is a global public health problem likely to grow in tandem with ageing of the global population. However, less attention has been focused on why it is happening and how it can be prevented.

Objective The objective of this paper is to synthesise qualitative studies that explore PIP in older patients, in an effort to understand why it happens from a prescriber's perspective and to generate a new theory to guide future interventional studies aimed at minimising it in older people. To date, there is no published systematic synthesis of this type.

Methods Papers were deemed suitable for inclusion if they used qualitative methods, explored some area of PIP in patients over 65 years of age, were published in English and had available published abstracts. Four databases were systematically searched for papers published up to the end of April 2013: PubMed, Embase, CINAHL and Web of Knowledge. No date restrictions were applied. Key words searched were: Qualitative AND (Inappropriate* OR Appropriate* OR Safe) AND (Elderly OR Aged OR Geriatric* OR Old*) AND Prescri*. Reference lists were then searched for other suitable papers. Critical Appraisal Skills Programme criteria were used to assess quality. Meta-ethnography was used to synthesise the papers.

Results Out of 624 papers identified, seven papers were deemed relevant. Four key concepts were identified as being causal factors in PIP: (1) the need to please the patient, (2) feeling of being forced to prescribe, (3) tension between prescribing experience and prescribing guidelines and (4) prescriber fear. These were re-interpreted in a line of argument synthesis indicating that some doctors have self-perceived restrictions with regard to prescribing appropriately because of a combination of factors, rather than any one dominant factor.

Conclusion Prevention of PIP may be favourably influenced by addressing the key interactive determinants of inappropriate prescribing behaviour.

Key Points

Qualitative work in the field of potentially inappropriate prescribing in older patients has never before been synthesised.

This meta-synthesis indicates that doctors often have self-perceived restrictions leading to a sense of powerlessness to prescribe appropriately because of a combination of factors.

Possible methods for empowering doctors to prescribe appropriately include educational interventions and improved communication between levels of care.

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1 Introduction

Potentially inappropriate prescribing (PIP) is commonly seen amongst the older population. There are various factors that make this group more susceptible to PIP, principally multiple co-morbidities and related polypharmacy [1, 2]. PIP includes both prescribing of potentially inappropriate medications (PIMs), i.e. introducing a medication that poses more risk than benefit when a safer alternative is available, as well as potential prescribing omissions (PPOs) [2–6], i.e. the omission of medications that would benefit the patient. In primary care, recent studies show that 20–40 % of older patients have experienced PIP [1–3]. The prevalence of PIP in these patients is 33–58 % in the hospital setting [4, 5] and rates of 44–70 % have been reported in long-term care facilities [6]. The common consequences of PIP are adverse drug reactions, adverse drug events, hospitalisation and inefficient use of resources [7–9].

Quantitative data such as these have highlighted the issue and attracted attention. However, very little attention has been focused on *why* it is happening. This paper aims to synthesise qualitative studies that explore PIP in older patients, using a meta-ethnographic approach, as developed by Noblit and Hare [10], in an effort to understand the psychological and behavioural basis of PIP applied to older people and to generate a new theory to guide future intervention studies aimed at PIP prevention. The few qualitative studies in the published literature have never previously been analysed in a meta-synthesis such as this before. Application of qualitative research methods in a variety of healthcare research domains [11] has provided important insights and understanding with relevance to clinical practice.

As with a meta-analysis of data from quantitative studies, a meta-synthesis of qualitative studies involves a recognised methodology for combining the themes from several studies. However, unlike a meta-analysis, a qualitative synthesis aims to interpret the thematic findings from the original studies so as to be able to generate a new all-encompassing theory not previously identified [11–14]. To do this, we chose a technique called meta-ethnography [10] for this meta-synthesis, which has been used to good effect in healthcare research [11, 14–16].

2 Methods

We used the seven-step model of meta-ethnography (Fig. 1), i.e.

In step 1, we agreed *a clear statement of the specific research question.*

In step 2, we developed a *search strategy* to identify suitable articles. Four databases were systematically searched for papers published up to the end of April 2013 (no start date was specified): PubMed, Embase, CINAHL and Web of Knowledge. The following terms were used: Qualitative AND (Inappropriate* OR Appropriat* OR Safe) AND (Elderly OR Aged OR Geriatric* OR Old*) AND Prescri*. We then searched the reference lists of papers located for other suitable papers that should be included in the meta-synthesis.

Papers were deemed suitable for inclusion if they used qualitative methods, explored some area of PIP in patients over 65 years of age, were published in English and had available published abstracts. Two researchers (SC and AF) then read articles that were deemed potentially relevant after the abstract review. Articles meeting inclusion criteria were included in the final review.

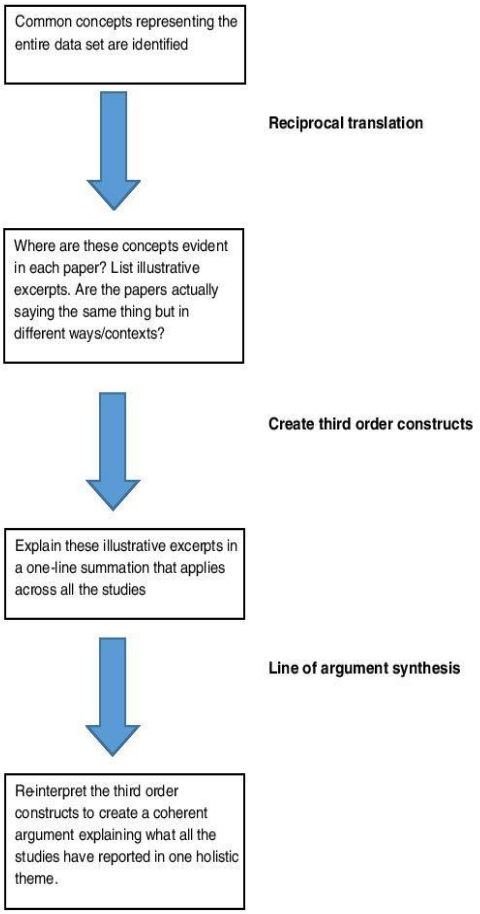


Fig.1 Flow diagram of meta-ethnography process

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The quality of the final papers was assessed by two researchers using the Critical Appraisal Skills Programme (CASP). The CASP tool assesses qualitative papers on the basis of the results presented, the validity of the results and the potential implications of the results locally. The authors decided to use the CASP methodology as it has been used to good effect previously in healthcare research studies [11, 13, 15, 17]. The purpose of using the CASP was not to eliminate published papers, but rather to make sure the papers we used were of high quality, and to ensure low-quality papers were not contributing to our final synthesis.

Step 3 involved *reading the studies*. The terms first-order, second-order and third-order constructs relate to the different levels of interpretation within a meta-synthesis. First-order constructs relate to the raw data in the empirical studies, i.e. the original participants' interpretations of a certain experience. Second-order constructs are the common themes/categories that the original authors identified amongst these participants and used as their results/findings. Third-order constructs are the *new* interpretations that those performing the synthesis must identify by compiling all the second-order constructs from the selected studies, translating them into each other to determine if in fact they concur in terms of thematic content, and then reinterpreting them to generate new theory. The papers were read carefully by two researchers. The key findings from each paper, as presented by the authors, were listed as the second-order constructs.

In step 4, we determined how the studies were related to each other by listing key concepts that represented the whole data set.

In step 5, we translated the papers into each other. There are numerous forms of final synthesis within meta-ethnography, the choice of which depends on how the papers are related to each other [10]. As it became apparent that concepts from one study would encompass others, if not all the other studies, the authors used 'reciprocal translation' followed by a 'line of argument' synthesis. Each key concept was compared across the published papers, to determine what each paper stated about that concept. In this way, the papers were translated into one another.

Step 6 involved examining what each paper stated about each concept, and reinterpreting these to produce third-order constructs, linked together in a final 'line of argument' synthesis. The aim of a 'line of argument' is to create a coherent theme that may explain what all the studies have reported in one holistic theme, taking into account the fact that each study may have explored different aspects of the phenomenon [18].

Finally, in step 7, we expressed the results of the synthesis in tables, figures and text. We used the ENTREQ (Enhancing transparency in reporting the synthesis of qualitative research) [19] statement, a framework for reporting the synthesis of qualitative health research, to guide how we reported the results.

3 Results

The search of the electronic databases identified 864 papers, leaving 624 after duplicates were removed (Fig. 2). After a title and abstract review, a further 576 were removed: 348 did not use qualitative methods, 176 did not involve PIP, 44 did not deal with patients over 65 years and eight had no abstracts available. Sixteen full papers were retrieved for review. Of these, ten were eliminated because they did not use qualitative methods. One additional paper was identified from the references list of another paper and included. This left seven papers for inclusion in the final synthesis (Table 1).

All seven papers were of high quality when assessed using the CASP criteria; all of the papers met most of the criteria for inclusion in the analysis. Common weaknesses were 'reflexivity' (the awareness of the *researcher's* contribution to the construction of meanings throughout the research process), which none of the papers mentioned, 'data collection' (none of the papers justified methods chosen or discussed saturation of data) and 'statement of

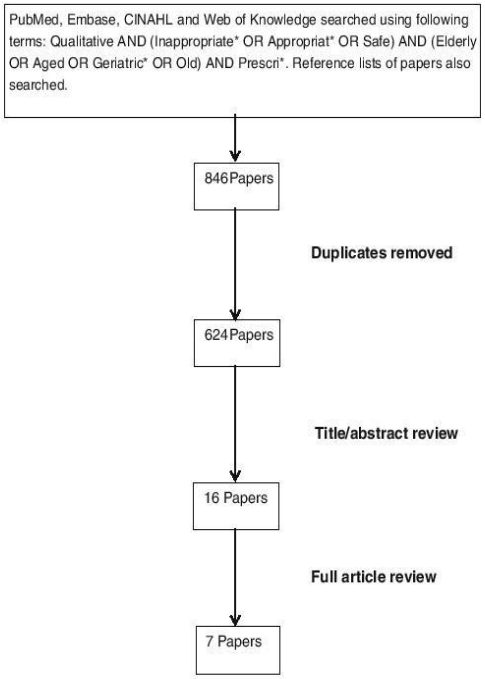


Fig. 2 PRISMA flow diagram of literature review process

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Table 1 Characteristics of papers identified

	Paper title (year of publication)	Reference	Country	Sample size (*n*)	Method
1.	Prescribing psychotropic medication for elderly patients: some physicians perspectives (1999)	Damestoy et al. [26]	Canada	Doctors (9)	Grounded theory, semi-structured interviews
2.	Appropriateness of use of medicines in elderly inpatients: qualitative study (2005)	Spinewine et al. [28]	Belgium	Doctors (5) Nurses (4) Pharmacists (3) Patients (17)	Grounded theory, semi-structured interviews, focus groups, observation
3.	Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study (2007)	Cook et al. [23]	USA	GPs (33)	Narrative analysis, semi-structured interviews
4.	GPs' approach to insulin prescribing in older patients: a qualitative study (2008)	Agarwal et al. [21]	Canada	GPs (21)	Grounded theory, semi-structured interviews
5.	Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study (2008)	Wood-Mitchell et al. [27]	England	Consultant psychiatrists (8)	Grounded theory, semi-structured interviews
6.	Long-term prescribing of antidepressants in the older population: a qualitative study (2010)	Dickinson et al. [20]	England	Patients (36) GPs (10)	Framework analysis, semi-structured interviews
7.	Primary care providers' perspective on prescribing opioids to older adults with chronic non-cancer pain: a qualitative study (2011)	Spitz et al. [22]	USA	Doctors (23) Nurse practitioners (3)	Thematic analysis, focus groups

findings' (the vast majority of papers did not apply triangulation).

3.1 Reciprocal Translation

Four key concepts that reflected the findings in the seven papers were identified from the meta-synthesis as being contributory factors to PIP: (1) desire to please the patient, (2) feeling of being forced to prescribe, (3) tension between experience and guidelines and (4) prescriber fear. The reciprocal translation and final synthesis are presented below. Each of these thematic concepts is described in greater detail. Excerpts consisting of original quotes from participants (first-order constructs) as well as authors' findings (second-order constructs), from the original papers are presented in Table 2 along with third-order interpretations to illustrate how the four themes were identified.

3.1.1 Please the Patient

In the majority of papers, there was a clear underlying theme of 'wanting to please the patient'. This usually meant prescribing outside the guidelines but as Dickinson et al. [20] stated in their paper exploring inappropriate long-term prescribing of antidepressants, '… in many circumstances it is easier to follow the path of least resistance and let them (i.e. PIP decisions) be…'. This was a common viewpoint expressed by the doctors they interviewed. They noted that patients were happy with their antidepressants and as a result doctors were generally satisfied with the pharmacotherapy. They also observed that the doctors recognised the problem of prescribing medication even though the problem may be social rather than psychiatric in nature. However, because of some patients' resistance to non-pharmacological treatments, they proceeded with prescribing the medication anyway.

Agarwal et al. [21] refers to this resistance from patients' in their study of general practitioners' (GPs') approach to insulin prescribing in older patients. When asked why insulin is often under-prescribed in this population, the consensus was that 'GPs felt older patients would be less receptive to medication regimen changes'. Spitz et al. [22] looked at underuse of opioids in older patients for non-cancer pain. In this study, the patient was also a common barrier to appropriate prescribing here, apparently as a result of older patients' reluctance to consider opioid analgesia for this category of pain. The physician participants in this study also commented that this resistance acted as a barrier to prescribing these medications to future patients.

The concept of prescribing to please the patient was most evident in the paper by Cook et al. [23] who explored prescribers' attitudes to prescribing benzodiazepines for older adults. These medications should only be used for brief periods in older patients and for symptomatic relief only [24, 25]. The participants in this study spoke of the problems they experienced in the past trying to wean patients off benzodiazepines and how this affected their

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Table 2 Excerpts supporting the four themes plus third-order interpretations

	Excerpts (first- and second-order constructs; first-order constructs in italics)	Paper(s)	Third-order interpretations
Desire to please the patient	They [antidepressants] allow the doctor and the patient a feeling of doing something in the face of unsolvable problems	Dickinson et al. [20]	The patient can have too much of a deciding role in their therapy at times. This sometimes hinders the doctor from making his/her decision based purely on what is the best course of action for the patient
	There appeared to be some sense of unease about prescribing a medical intervention for a social cause … the goal of both doctor and patient appears to not rock the boat	Dickinson et al. [20]	
	Prospects ranged from questioning the doctor's authority and competence, to minimisation of negative side effects, to finding another doctor who was willing to prescribe it	Cook et al. [23]	
	Many of the physicians thought patients would seek out another physician if they were not satisfied with their prescription, and they took this into account before prescribing	Damestoy et al. [26]	
Feeling forced to prescribe	Some participants felt that certain homes coped better than others with problematic behaviours and one thought it depended on whether beds needed to be filled	Wood-Mitchell et al. [27]	Because of a combination of intrinsic and extrinsic factors, and although they may realise it is not quite appropriate, doctors are sometimes left with no other choice but to prescribe, or not prescribe, in an inappropriate fashion
	GPs also described situations where their own experiences or knowledge of particular nursing homes or less-than-ideal care situations, hindered them from considering insulin treatment	Agarwal et al. [21]	
	All participants felt strongly that there was a pressure to prescribe … (that) the availability of alternatives to medication influenced decisions	Wood-Mitchell et al. [27]	
	One frequently cited reason for the favouring of antidepressants was the inadequacy or unavailability of alternative treatments	Dickinson et al. [20]	
	They recognised that the inappropriate use of psychotropic medication for older patients was a public health problem, but they felt it was beyond the scope of the individual physician	Damestoy et al. [26]	
Experience vs. guidelines	In most cases, choice of medication was based on familiarity and past experience of a drug … the influence of an evidence base had a varying effect on the participants	Woods-Mitchell et al. [27]	Past experience, or lack thereof, can sometimes over-ride guidelines or the appropriate decisions. Sometimes this may simply be necessary and actually appropriate; however, the literature suggests it is also contributing to potentially inappropriate prescribing
	Most GPs had little experience of treating older patients with insulin. This lack of experience made some apprehensive about initiating it	Agarwal et al. [21]	
	In the absence of evidence of specific adverse effects, there was little concern	Dickinson et al. [20]	
Prescriber fear	Two doctors acknowledged that information transferred to general practitioners could be limited by fear of offending them with comments on inappropriate prescribing	Spinewine et al. [28]	Fear is a multifactorial component of potentially inappropriate prescribing. While not likely to be the major cause of inappropriate prescribing, it would seem to compound already existing factors, thereby contributing to the overall effect
	"It's scary to stop a medication that's been going on a long time, because you think am I opening a can of worms here"	Dickinson et al. [20]	
	"I get frightened with 80+ year olds; how are they going to respond?"	Spitz et al. [22]	

future prescribing patterns. The participants again spoke of 'the path of least resistance' and how much quicker and easier it is just to prescribe what the patient wants, rather than spend significant amounts of time trying to persuade patients that a different approach to managing insomnia and anxiety would be preferable. They furthermore

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identified the possibility of the patients switching to another physician as a reason for inappropriate prescribing. This was also reported by Damestoy et al. [26], who studied physicians' perspectives on prescribing psychotropic medication for older patients. The participants described how otherwise quiet and timid patients became aggressive and demanding when their anxiolytic use was questioned.

3.1.2 Forced to Prescribe

One consequence of this need to please the patient was that prescribers often felt they were forced into prescribing, or not prescribing medications, in a manner they knew did not adhere to guidelines. This concept could therefore have been integrated into the previous one; however, we consider it should stand alone, as there were several factors leading prescribers to feeling forced to prescribe, other than the need to please the patient, e.g. poor quality of treatment resources. Wood-Mitchell et al. [27] explored prescribing of medications for dementia in older patients. They observed that many of the prescribers felt they were seeing too many referred patients owing to a lack of support services for these patients. According to many prescribers, there was too much reliance on medication as a quick and 'easy' treatment for these patients and the development of non-pharmacological treatments was deployed less frequently as a result. Additionally, the quality-of-care settings were important in the prescribers' decision process. Low-quality care staff training and 'under-stimulating environments' were thought to result in challenging behaviours in patients with dementia. These low-quality care facilities are then unable to cope with disturbed patient behaviour and are more likely to refer the patients for assessment with a view to pharmacotherapy for their disturbed behaviour. The physician prescribers then feel they have no choice but to prescribe owing to the lack of services already mentioned.

Agarwal et al. [21] also reported this lack of confidence amongst prescribers in some long-term care settings. In relation to not prescribing insulin, GPs knowledge of some care facilities hindered them from starting a patient on insulin because of the doctor's lack of confidence in the support the patient would receive in care. Lack of alternatives was another factor leading to physicians feeling forced to prescribe something. Damestoy et al. [26] described how doctors felt that non-pharmacological treatments were insufficient for conditions such as anxiety, indicating that many doctors 'considered them to be ineffective (and that) … psychotherapeutic approaches were doomed to failure'. This was echoed by Wood-Mitchell et al. [27], and again by Dickinson et al. [20], indicating long waiting lists for cognitive behavioural therapy. Damestoy et al. [26] also identified a feeling of isolation amongst prescribers, once again forcing them to prescribe in some situations where they realize that psychotropic medications are not appropriate. This theme of 'isolation' was also picked up by Spitz et al. [22] reporting that doctors desired more peer support to enable them to prescribe appropriately. Looking at these studies, it can be seen that prescribers know what is right, but feel unable to follow through.

3.1.3 Experience vs. Guidelines

In all but one of the papers, it was clear that prescribers were well aware of the potentially inappropriate nature of some of their prescribing. They were, for the most part, aware of the treatment guidelines and they all agreed as to what the best practice was. However, in general, they varied greatly in their actual practice. They perceived a significant problem in implementing these guidelines in real life. The end result was reversion to previous practices, and what they were familiar with. Lack of evidence supporting some guidelines also influenced prescribers in favour of their own experience as reported by Woods-Mitchell et al. [27]. Conversely, Agarwal et al. [21] reported that a prescriber's *lack* of experience can have a similar effect in relation to under-prescribing of insulin.

Cook et al. [23] found that many prescribers considered that guidelines were 'out of touch with real-world problems' and that past experience had taught them to avoid changing drug therapy to avoid a perceived higher risk of misadventure. Damestoy et al. [26] reported that many of the physicians interviewed prescribed as they did because they did not often see adverse effects. Spitz et al. [22] used focus groups with prescribers to elucidate why opioids were underused in non-cancer pain in older people. They found that doctors were aware that opioids have a role in non-cancer pain, but felt the evidence base was insufficient to support this role. They also expressed their desire for evidence-based tools for calculating doses. Dickinson et al. [20] showed that in relation to long-term prescribing of antidepressants, GPs did not see much of a problem, as they have not seen any evidence to indicate serious harm to older patients.

3.1.4 Fear

The final concept evident across the papers reviewed was fear. It manifested itself in a number of different ways but in all cases it was clear that it was a contributing factor to PIP. For instance, Agarwal et al. [21] reported that doctors felt a sense of fear toward older patients in general owing to their frailty and co-morbidities. Consequently, they perceived more potential to do harm. They also observed a

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fear of the unknown amongst several GPs, e.g. most admitted to inexperience using insulin in older patients and found the prospect of initiating it anxiety provoking, such that they would avoid prescribing it even if guidelines recommended it. Dickinson et al. [20] also identified fear as a central theme amongst GPs in relation to PIP. Doctors described reluctance to stopping a medication that has been taken for a long time by a patient to avoid worry, and spoke of not wishing to disrupt patients' clinical stability. With this fear of medication change and an apparent lack of fear of adverse effects (also reported), these authors concluded that there was no incentive for change. Fear of causing harm was the overwhelming barrier identified in the study by Spitz et al. [22]. Prescribers described genuine fear of prescribing opioids for older patients, and worry regarding the possible serious adverse effects. Sometimes these fears arose from previous bad experiences with prescribing opioids in older patients. In other cases, this fear was more to do with avoidance of the guilt that would ensue if a patient was to have an adverse drug event because of the drug. Spinewine et al. observed a different type of fear in their study looking at appropriateness of medicines in general in older patients [28]. Prescribers they interviewed described a fear of offending other doctors, including specialist doctors and GPs. If, for example, a doctor noticed something potentially inappropriate on a patient's prescription, but if that patient was under the care of a specialist, they would be less likely to intervene. Similarly, when transferring information between levels of care, e.g. from hospital to primary care, it was noted that the amount of information could be limited because of fear of causing offence to patients' GPs.

3.2 Line of Argument Synthesis

Looking at the four key concepts that emerged from the papers, we concluded that the literature actually indicates that, in many situations, prescribers suffer from 'self-perceived restrictions' leading to a sense of powerlessness to prescribe appropriately for older patients. This forces them to rely on what they know and have done before, which leads to the PIP that has been identified [4–8].

4 Discussion

Although the published literature abounds with papers describing the prevalence of PIP in various clinical settings and the link between PIP and multi-morbidity/polypharmacy in older people, there is a lack of scientific enquiry into the prescriber-based reasons that underpin PIP. This meta-synthesis has, for the first time, identified a cluster of reasons physicians feel may perpetuate PIP in older people. These reasons include (1) the need to please the patient, (2) feeling forced to prescribe, (3) tension between prescribing experience and prescribing guidelines and (3) prescriber fear. Ultimately, these factors in combination militate against safe and effective prescribing in older people.

To date, there is a lack of proven interventions that reliably counteract PIP in older patients. A recent review by O'Connor et al. [5] points toward four areas of intervention to counteract PIP in this population, namely comprehensive geriatric assessment, medication use review, prescriber education/audit/feedback and computerised prescriber order entry with clinical decision support. However, the evidence to support routine implementation of any of these interventions to prevent PIP in multi-morbid older patients is weak. Prescriber education interventions to prevent PIP in particular drug classes have been shown to work, e.g. antibiotics, opioid analgesics and antipsychotics [5]. However, interventions to guide prescribers away from PIP in the broad sense are lacking. Rather surprisingly, researchers have given relatively little attention to the *prescriber* as a prime target for attenuating PIP in the high-risk, older, multi-morbid population.

Whilst there may be other prescriber factors to consider other than the four prime reasons that predispose physicians to poor prescribing practices identified in this study, nevertheless, our findings provide an evidence-based platform for the design of more effective interventions as a means of PIP prevention in older populations. Whatever interventions are developed in the future, they must be able to empower physicians to prescribe in such a way as to improve adherence to guidelines, avoid feelings of being forced to prescribe inappropriately to please patients and fear of countermanding other physicians prescriptions.

The global expansion of the frail older population demands an improved level of education in geriatric pharmacology at the undergraduate and postgraduate level. Specifically, this will involve electronic education programmes that include self-testing and feedback. Importantly, recent discourse on prescriber 'non-technical skills' has cast new light on a previously neglected aspect of prescriber behaviour [29]. These 'non-technical skills' encompass communication, team-working/leadership, error awareness, risk assessment and situational awareness. This skill set must be incorporated into any prescriber education programme to enhance its efficacy. A model for the delivery of such an intervention has been suggested [29].

4.1 Limitations

Although we systematically searched for suitable papers, qualitative papers are often difficult to find because of ambiguous titles.

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Meta-ethnography, while a useful tool for this type of research, is not an objective technique and is open to differing interpretations between different researchers.

Four of the seven papers included in this review concerned the prescribing of psychiatric medications. Mediators of PIP may differ between psychiatry and general medicine. Similarly, the mediators of the different forms of PIP (PIMs and PPOs) may differ. PIMs and PPOs were not separated for individual analysis in this paper.

5 Conclusion

PIP in older patients is a result of many factors, including patient-, prescriber- and system-level barriers. As a result, prescribers feel unable to prescribe in an appropriate manner. Possible remedies for this could include better communication, more comprehensive education and system-level interventions to enable prescribers to re-acquire this power. The problem is not a lack of guidelines, it is an abundance of barriers to implementing these guidelines, which need to be systematically removed.

Acknowledgments The authors would like to acknowledge the Health Research Board of Ireland for funding this research (Grant no. HRA_HSR/2010/14). The manuscript does not contain clinical studies or patient data.

Conflict of interest The authors declare no conflict of interest.

References

1. Ryan C, O'Mahony D, Kennedy J, et al. Potentially inappropriate prescribing in an Irish elderly population in primary care. Br J Clin Pharmacol. 2009;68(6):936–47.
2. Dunn RL, Harrison D, Ripley TL. The Beers criteria as an outpatient screening tool for potentially inappropriate medications. Consult Pharm. 2011;26(10):754–63.
3. Spiker EC, Emptage RE, Giannamore MR, et al. Potential adverse drug events in an indigent and homeless geriatric population. Ann Pharmacother. 2001;35(10):1166–72.
4. Gallagher P, Lang PO, Cherubini A, et al. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. Eur J Clin Pharmacol. 2011;67(11):1175–88.
5. O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. Drugs Aging. 2012;29(6):437–52.
6. O'Sullivan DP, O'Mahony D, Parsons C, et al. A prevalence study of potentially inappropriate prescribing in Irish long-term care residents. Drugs Aging. 2013;30(1):39–49.
7. Lund BC, Carnahan RM, Egge JA, et al. Inappropriate prescribing predicts adverse drug events in older adults. Ann Pharmacother. 2010;44(6):957–63.
8. Chrischilles EA, VanGilder R, Wright K, et al. Inappropriate medication use as a risk factor for self-reported adverse drug. J Am Geriatr Soc. 2009;57(6):1000–6.
9. Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: inappropriate prescription is a leading cause. Drugs Aging. 2005;22(9):767–77.
10. Noblit GW, Hare RD. Meta-ethnography: synthesising qualitative studies. New York: Sage; 1988.
11. Campbell R, Pound P, Pope C, et al. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. Soc Sci Med. 2003;56(4):671–84.
12. Campbell R, Pound P, Morgan M, et al. Evaluating meta-ethnography: systematic analysis and synthesis of qualitative research. Health Technol Assess. 2011;15(43):1–164.
13. Atkins S, Lewin S, Smith H, et al. Conducting a meta-ethnography of qualitative literature: lessons learnt. BMC Med Res Methodol. 2008;16(8):21.
14. Malpass A, Shaw A, Sharp D, et al. "Medication career" or "moral career"? The two sides of managing antidepressants: a meta-ethnography of patients' experience of antidepressants. Soc Sci Med. 2009;68(1):154–68.
15. Pound P, Britten N, Morgan M, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. Soc Sci Med. 2005;61(1):133–55.
16. Britten N, Campbell R, Pope C, et al. Using meta ethnography to synthesise qualitative research: a worked example. J Health Serv Res Policy. 2002;7(4):209–15.
17. Teixeira Rodrigues A, Roque F, Falcao A, et al. Understanding physician antibiotic prescribing behaviour: a systematic review of qualitative studies. Int J Antimicrob Agents. 2013;41(3):203–12.
18. Thorne S, Jensen L, Kearney MH, et al. Qualitative metasynthesis: reflections on methodological orientation and ideological agenda. Qual Health Res. 2004;14(10):1342–65.
19. Tong A, Flemming K, McInnes E, et al. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Med Res Methodol. 2012;27(12):181.
20. Dickinson R, Knapp P, House AO, et al. Long-term prescribing of antidepressants in the older population: a qualitative study. Br J Gen Pract. 2010;60(573):257–9.
21. Agarwal G, Nair K, Cosby J, et al. GPs' approach to insulin prescribing in older patients: a qualitative study. Br J Gen Pract. 2008;58(553):569–75.
22. Spitz A, Moore AA, Papaleontiou M, et al. Primary care providers' perspective on prescribing opioids to older adults with chronic non-cancer pain: a qualitative study. BMC Geriatr. 2011;14(11):35.
23. Cook JM, Marshall R, Masci C, et al. Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study. J Gen Intern Med. 2007;22(3):303–7.
24. Salzman C, The APA. Task Force report on benzodiazepine dependence, toxicity, and abuse. Am J Psychiatry. 1991;148(2):151–2.
25. Consensus conference. Drugs and insomnia: the use of medications to promote sleep. JAMA. 1984;251(18):2410–4.
26. Damestoy N, Collin J, Lalande R. Prescribing psychotropic medication for elderly patients: some physicians' perspectives. CMAJ. 1999;161(2):143–5.
27. Wood-Mitchell A, James IA, Waterworth A, et al. Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study. Age Ageing. 2008;37(5):547–52.
28. Spinewine A, Swine C, Dhillon S, et al. Appropriateness of use of medicines in elderly inpatients: qualitative study. BMJ. 2005;331(7522):935–8.
29. Gordon M. Non-technical skills training to enhance patient safety. Clin Teach. 2013;10(3):170–5.

11.2 Appendix II: CASP checklist for qualitative studies



10 questions to help you make sense of qualitative research

How to use this appraisal tool

Three broad issues need to be considered when appraising the report of a qualitative research:

- **Are the results of the review valid?**
- **What are the results?**
- **Will the results help locally?**

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

These checklists were designed to be used as educational tools as part of a workshop setting

There will not be time in the small groups to answer them all in detail!

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Screening Questions

1. Was there a clear statement of the aims of the research?

❑ Yes ❑ Can't tell ❑ No

HINT: Consider

- What was the goal of the research?
- Why it was thought important?
- Its relevance

---

2. Is a qualitative methodology appropriate?

❑ Yes ❑ Can't tell ❑ No

HINT: Consider

- If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants
- Is qualitative research the right methodology for addressing the research goal?

Is it worth continuing?



Detailed questions

3. Was the research design appropriate to address the aims of the research? ❑ Yes ❑ Can't tell ❑ No

HINT: Consider

- If the researcher has justified the research design (e.g. have they discussed how they decided which method to use)?

---

4. Was the recruitment strategy appropriate to the aims of the research? ❑ Yes ❑ Can't tell ❑ No

HINT:Consider

- If the researcher has explained how the participants were selected
- If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
- If there are any discussions around recruitment (e.g. why some people chose not to take part)

5. Was the data collected in a way that addressed the research issue? ❑ Yes ❑ Can't tell ❑ No

HINT: Consider

- If the setting for data collection was justified
- If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
- If the researcher has justified the methods chosen
- If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews were conducted, or did they use a topic guide)?
- If methods were modified during the study. If so, has the researcher explained how and why?
- If the form of data is clear (e.g. tape recordings, video material, notes etc)
- If the researcher has discussed saturation of data

---

6. Has the relationship between researcher and participants been adequately considered? ❑ Yes ❑ Can't tell ❑ No

HINT: Consider

- If the researcher critically examined their own role, potential bias and influence during
  (a) Formulation of the research questions
  (b) Data collection, including sample recruitment and choice of location
- How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

7. Have ethical issues been taken into consideration? ❑Yes ❑Can't tell ❑No

HINT: Consider

- If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained
- If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study)
- If approval has been sought from the ethics committee

---

8. Was the data analysis sufficiently rigorous? ❑Yes ❑Can't tell ❑No

HINT: Consider

- If there is an in-depth description of the analysis process
- If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data?
- Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process
- If sufficient data are presented to support the findings
- To what extent contradictory data are taken into account
- Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation

9. Is there a clear statement of findings?

❒ Yes ❒ Can't tell ❒ No

HINT: Consider

- If the findings are explicit
- If there is adequate discussion of the evidence both for and against the researchers arguments
- If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst)
- If the findings are discussed in relation to the original research question

---

10. How valuable is the research?

HINT: Consider

- If the researcher discusses the contribution the study makes to existing knowledge or understanding e.g. do they consider the findings in relation to current practice or policy?, or relevant research-based literature?
- If they identify new areas where research is necessary
- If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

11.3 Appendix III: PRISMA checklist for systematic reviews

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

11.4 Appendix IV: Doctors' perspectives on the barriers to appropriate prescribing in older hospitalised patients: A qualitative study

BJCP British Journal of Clinical Pharmacology

DOI:10.1111/bcp.12555

Doctors' perspectives on the barriers to appropriate prescribing in older hospitalized patients: a qualitative study

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Keywords
inappropriate, older patients, potentially, prescribing, qualitative

Received
13 August 2014
Accepted
12 November 2014
Accepted Article Published Online
18 November 2014

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT?

- Potentially inappropriate prescribing (PIP) is a significant problem in the older population.
- PIP is associated with many negative outcomes, including the occurrence of adverse drug events (ADEs) and hospitalization.
- While much research has explored the prevalence of PIP, little work has been done to identify why it occurs.

WHAT THIS STUDY ADDS

- Doctors feel they do not receive sufficient training in prescribing for older patients.
- Doctors are aware that PIP occurs but often feel forced to prescribe even though they know it may be inappropriate.
- Interventions to address PIP will have to be multi-faceted.

AIMS

Older patients commonly suffer from multimorbidites and take multiple medications. As a result, these patients are more vulnerable to potentially inappropriate prescribing (PIP). PIP in older patients may result in adverse drug events (ADEs) and hospitalizations. However, little has been done to identify why PIP occurs. The objectives of this study were (i) to identify hospital doctors' perceptions as to why PIP occurs, (ii) to identify the barriers to addressing the issues identified and (iii) to determine which intervention types would be best suited to improving prescribing.

METHODS

Semi-structured interviews based on the Theoretical Domains Framework (TDF), a tool used to apply behaviour change theories, were conducted with 22 hospital doctors. Content analysis was conducted to identify domains of the TDF that could be targeted to improve prescribing for older people. These domains were then mapped to the behaviour change wheel to identify possible intervention types.

RESULTS

Content analysis identified five of the 12 domains in the TDF as relevant: (i) environmental context and resources, (ii) knowledge, (iii) skills, (iv) social influences and (v) memory/attention and decision processes. Using the behaviour change wheel, the types of interventions deemed suitable were those based on training and environmental restructuring.

CONCLUSION

This study shows that doctors feel there is insufficient emphasis on geriatric pharmacotherapy in their undergraduate/postgraduate training. An intervention providing supplementary training, with particular emphasis on decision processes and dealing with social influences would be justified. This study has, however, uncovered many areas for potential intervention in the future.

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Introduction

It is a well-known phenomenon that the population is ageing globally. Recent projections estimate that by 2018, there will be more people over the age of 65 years than there will children under 5 years worldwide [1]. By 2040, 1.3 billion people will be over 65 years of age, an increase from the current 7% of the worlds' population to 14% [1]. Advances in diagnostics, treatment, and in healthy living initiatives are largely responsible for this population growth [1]. The prescribing of multiple medications for multiple disease states, is common amongst older individuals, and these patients are therefore more vulnerable to medication related problems, including potentially inappropriate prescribing (PIP) [2, 3]. PIP is defined as either the prescribing of a medicine that carries more risk than benefit, especially when there is a safer alternative, or the omission of a medicine that would be of benefit to the patient [2–6]. Studies conducted in Ireland and continental Europe show that PIP is a significant problem, with prevalence rates of 20%, 58% and 70% reported in primary, secondary and tertiary care, respectively [7–11]. PIP is associated with many negative outcomes, including the occurrence of adverse drug events (ADEs) and hospitalization, and consequently places a large economic strain on the health care system and intangible costs on individuals.

Whilst it is acknowledged in the literature that PIP is an issue requiring significant attention, little qualitative research has been conducted into why PIP occurs. Indeed, studies investigating PIP have traditionally focused on the individual medicines or pharmacological class of medicines that are inappropriately prescribed [12–17].

Behavioural change is key to any intervention requiring improvement in clinical practice. Behaviour change interventions can be modelled on any number of evidence-based theories that exist within health psychology [18, 19]. However, with so many to choose from, there is always doubt as to whether the model chosen fully accounts for the behaviour in question. A solution has been presented for this problem. An overarching theoretical framework, combining 128 constructs from 33 theories of behaviour change was developed by Michie *et al.* [20]. The resultant framework, known as the 'Theoretical Domains Framework' (TDF) consists of 12 'theoretical domains'. These domains serve as potential mediators of change.

In the UK, the PROTECT study (PRescribing Outcomes for Trainee doctors Engaged in Clinical Training) investigated the prevalence and causes of prescribing errors made by junior doctors. As part of this, Duncan *et al.* used the TDF to explore the factors that influence junior doctors' prescribing behaviour [21]. They found seven domains to be likely mediators of change and using previously published methods [22], suggested several behaviour change techniques likely to be useful in an intervention study [21]. Similarily, in order to implement changes in current prescribing practice for older people, it is necessary to identify the processes leading to the prescribing of inappropriate medicines. Further examination of the barriers and facilitators to these processes will allow for effective implementation of prescribing improvement interventions.

The aims of this study were using the TDF, (i) to explore hospital doctors' perceptions as to why PIP occurs, (ii) to identify the barriers to addressing the issues identified, thus identifying potential targets for intervention and (iii) to use the behaviour change wheel to determine which intervention types would be best suited.

Methods

Sampling

In Ireland, there are three types of hospitals, (i) public hospitals, owned and funded by the Health Service Executive (HSE), (ii) voluntary hospitals, which are run by voluntary/private boards who receive money from the government to provide health care services and (iii) private hospitals who receive no state funding. Hospitals were purposively selected to ensure a range of hospital type were included in the study, large HSE, small HSE, large voluntary and small voluntary.

A sampling matrix was designed to ensure our participant sample was representative of doctors prescribing for older people in the hospital setting and represented doctors working in both geriatrics and in general medicine. The matrix ensured we interviewed an equal number of doctors of each grade, both from geriatrics and general medicine, and from each hospital.

Convenience sampling was then used to identify study participants within the hospitals. The chosen hospitals, in the Munster region of Ireland, were contacted and asked if they would take part in the study. The chief hospital pharmacist was the point of contact in all hospitals, and approached hospital doctors on our behalf. They were provided with a written description of the study's background, aims and methods, and were asked to pass this information to hospital consultants. Consultants were asked if they would make themselves and their team available for a 25–30 min one-on-one interview. The primary researcher (SC) then followed up with an e-mail within 1 week of the initial contact by the chief pharmacist. Consultants willing to participate approached each member of their team informing them of the study and provided details of those team members who were willing to participate in the research. Doctors were excluded if they were working in surgery involved in research related/similar to this study (currently or in the past), or they had a pharmacy degree prior to undertaking their medical training.

Data collection

Semi-structured interview topic guides were formulated by the research team based on the TDF. The original 12

domain TDF was used [20], due to its proven track record and use in similar studies [20, 21, 23, 24]. The interview schedule was then piloted with three health care professionals and amended accordingly.

Semi-structured interviews were the preferred method of data collection as it is well established that semi-structured interviews tend to delve deeper into the core of a subject and elicit more meaningful responses from participants [25].

The purpose of the topic guide was to explore the 12 domains of the TDF, while also allowing participants to speak freely, unlimited by strict questions. It has been shown that interviews based on the TDF elicit responses from participants that would not otherwise be reported [26].

Participants were briefed about the study and reassured that all interviews would be anonymized. Demographic details were collected before the interview, including grade, gender, number of years working as a doctor, his/her current speciality, details of any specific training in geriatric medicine they may have received and university attended. Interviews were audio-recorded and later transcribed verbatim. They were also asked some general questions regarding their knowledge and awareness of PIP.

Interview locations included a private hospital office used for various research projects, consultants' private offices, hospital canteens and doctors' lounges. All locations were on hospital grounds to minimize disruption to participants.

Data analysis

A similar approach adopted by Duncan *et al*. [21] was followed for this study as a similar behaviour was being described i.e. prescribing. All transcripts were inputted into QSR NVivo® Version 10 to facilitate analysis. Analysis was conducted in two phases. Phase 1 was a familiarization phase, where transcripts were read and re-read to ensure that researchers were familiar with the entire content of all transcripts [27]. In phase 2, conventional content analysis [28] was conducted independently by two researchers (SC and AF). In conventional content analysis, the researchers identified themes within the transcripts, and coded all subsequent texts to these themes as they arose. Findings were compared and differences resolved through further discussion, analysis and consensus [29].

Directed content analysis [28] was then employed to apply the TDF and identify relevant domains. In directed content analysis, unlike conventional, texts were coded to a pre-defined list of domains or research findings. Using the TDF helps to define a behaviour and identify barriers and facilitators to that behaviour. The TDF has been employed in a wide range of health care related research to inform better future intervention [21, 23, 24] and has since been expanded to 14 domainis [30]. Once domains within the TDF are identified, they can be mapped to suitable intervention types using the 'behaviour change wheel', a previously published technique also developed by Michie *et al.* [31]. A domain was deemed relevant if text from the interview transcripts was frequently coded into that domain *and* participants suggested that constructs within the domain were an influencing factor in PIP. Again, the domains identified as relevant were agreed upon by two researchers (SC and AF). The behaviour change wheel [31] was then used to identify intervention types that would be suitable, given the domains identified.

The authors decided to use two forms of content analysis to ensure that all relevant themes were identifed. For the purposes of the study and identifying domains to be targeted in a future intervention, the directed content analysis was to be the primary data source. The conventional content analysis was to be used to identify other, less critical areas of interest that may arise but not fit directly into the TDF.

Ethics approval for this study was sought from and granted by the Clinical Research Ethics Committee in University College Cork, Republic of Ireland.

Results

All doctors approached to take part, did so and a total of 22 interviews were conducted.

Four hospitals took part, two HSE and two voluntary (one large and one small of each), as well as all grades of doctor (Table 1). Thematic saturation was reached after 18

Table 1

Participant characteristics

Hospitals	Total number of participants from each	Grades of participants	Total number of participants working in geriatrics	Gender
Large HSE	6	2 Intern 2 SHO 2 Reg 1 Consultant	2	3 Male 3 Female
Small HSE	5	1 Intern 2 SHO 1 Reg 1 Consultant	3	3 Male 2 Female
Large voluntary	6	1 Intern 2 SHO 1 Reg 2 Consultant	3	4 Male 2 Female
Small voluntary	5	1 Intern 1 SHO 1 Reg 1 Consultant	2	2 Male 3 Female

Intern 1st year as qualified doctor; SHO: Senior House Officer (Next stage after Intern); Registrar (Reg) Next stage after SHO.

interviews but another four were carried out to ensure no new themes were emerging, as per the Francis method [32].

As mentioned above, the topic guide used for the interviews was designed to explore the domains of the TDF. However it also included some questions designed to provide a cross-sectional picture of doctors' awareness of PIP and prescribing in general for older patients. Some points of interest from these questions follow. (i) When asked to estimate what they thought the prevalence of PIP in hospitals was, the vast majority guessed above 50%. (ii) When asked if they thought it was a problem that needed addressing, all but one felt it was. (iii) When asked where they thought PIP might be most prevalent, primary, secondary or tertiary care 14 felt it was highest in primary care, (where it has actually been shown to be lowest (7–11)). (iv) When asked to rate their confidence in prescribing for older patients on a scale of 1–10 (10 being the most confident), over half placed it at between 5 and 6. These were all interns and senior house officers (SHOs). (v) When asked if they were aware of any screening tools to aid prescribing for older patients, only the consultants were able to name the common ones. The other participants, for the most part had heard of them but had no idea what they were.

Approximately half the doctors interviewed were, at time of interview, working in geriatrics (Table 1), with the remaining in other medical specialities or general medicine. The vast majority of doctors in geriatrics mentioned, without prompting or direct questioning on the matter, that prescribing within geriatrics is in general, far more appropriate than in other medical specialities they have experienced. There was a common trend within this group that more exposure to geriatricians would be of great benefit to prescribing in older patients, and this was also echoed by doctors not currently in geriatrics.

Conventional content analysis

Following familiarization, and open coding, four overarching themes, contributing to PIP were identified. They were;

- More education required in area of geriatric pharmacotherapy.
- Prescribing environment is conducive to PIP,
- Poor information technology (IT) infrastructure,
- Lack of collaboration between levels of care,

Directed content analysis

To identify relevant domains in the TDF that could be targeted in an intervention, directed content analysis was employed. In all, five domains were identified as relevant; environmental context and resources, memory/attention and decision processes, knowledge, skills and social influences. These same domains were identified from both the geriatricians' interview transcripts and those not working in geriatrics. Behaviour regulation and beliefs about capabilities were also identified at an early stage. However, although purported to in some interviews, they were not indicated as being a significant contributory factor in PIP. How each of the five relevant domains were represented is presented below. Knowledge and skills are presented together as participants made little distinction between the two. More quotes supporting the different domains are presented in Table 2.

Environmental context and resources The environment in which doctors prescribe was noted throughout the interviews, with interviewees reporting that the circumstances in which they prescribe create an atmosphere conducive to PIP. In particular, their workload, being interrupted while writing prescriptions and a lack of supportive IT infrastructure within their working environment, were considered conducive to PIP. They identified the multidisciplinary team structure as a definite facilitator to appropriate prescribing, but indicated that its impact is hampered by inefficient use of the resources within this team.

'That's a major problem. What you want to do when you're writing out a drugs kardex [prescription chart], is to be on your own, to be left alone, for 5 min while you just write out the thing. But it's actually an ideal opportunity for anybody who wants a piece of you for advice or whatever, (. . . .) nobody respects that at all, and nursing staff will use it as an opportunity to unload multiple other problems' **Site 1, interview 6 (Intern)**

A theme evident throughout many of the interviews was that of resources available, with particular emphasis on the lack of IT infrastructure. Interviewees noted that improvements and developments in the IT infrastructure could lead to much safer and more appropriate prescribing, with many doctors emphasizing that prioritizing improvement initiatives around IT infrastructure could have the most significant impact.

'Part of the reason (for PIP) is there isn't a very good interface between the electronic systems that they [GPs] use and the electronic systems that we use. So in an ideal world the GPs should be able to electronically send in all up to date information.' **Site 3, interview 2 (Consultant).**

A further issue raised by the interviewees, was the team support within the hospital environment. Particularly, the hospital pharmacist was considered a useful team member and a reliable resource. However, interviewees felt that the pharmacist's input was not used to full effect, with many not having regular pharmacist input. Some interviewees also noted that the way in

Table 2

Supporting quotes from interviews

TDF domain and intervention types identified as suitable by the behavior change wheel	Supporting quotes
1. Environmental context and resources **Behaviour change wheel interventions identified:** **-Environmental re-structuring** **-Persuasion** **-Incentivization**	*'I do think though, it's a tough job, it really is very tough, you're just flat out busy all the time, I think a lot of times you're just transcribing things you just go into auto pilot and you transcribe things that have already been prescribed and you don't question it.'* **Site 3, interview 1 (Intern)** *'We should have open access computers on every ward for resources including BNFs and other sorts of policy documents, antimicrobial policy and other things you use all the time. And these are all barriers, if you're unsure about checking the medication, these are all barriers that will put a lazy person off um, checking it. I think it's really important that we have better access to IT on every ward. It's really terrible at the moment.'* **Site 1, interview 6 (Intern)** *'I think it* [improved IT inifrastructure] *is a resource that would be potentially brilliant for drug and prescribing management, in general. How could I give you a better example of that now.. . ..I think let's say in community, in retail pharmacy, there are platforms available which off the bat* [straight away], *will flag drug–drug interactions, as you fill a script, and it's up to the pharmacist to look at it. We don't have anything like that, and it would be so easy.'* **Site 1, interview 6 (Intern)** *'In New Zealand we had a pharmacist for every team in the hospital who used to go around and check all the meds and they were very much part of the medical team and we took a lot of advice from them because they had more time to go through them* [the medicines prescribed]. *I know like the culture here is kind of, that we* [prescribers] *are in charge of meds, but that was one thing that was brill, and it wasn't just a green thing on the front of the chart, they would go through every admission, which was a big job, but they would go through every patient and go on the ward round, and they would have a medical idea of why the patient was in and recommend changes to the medications. I thought that was very good. The team didn't have to take the advice. Pharmacists are better at that kind of thing so I think that would be a really good idea'* **Site 1, interview 1 (Reg)** *'I think that actually, I do think pharmacists have helped me an awful lot this year. Like things like pointing out drug interactions that you mightn't have noticed (. . ..) definitely find the pharmacist really helpful so I don't mind them ringing me and their notes are great on the kardexes [prescription chart] and stuff. And it's especially helpful if there's something the patient can't remember'.* **Site 4, interview 6 (Intern)** *'Well we don't have clinical pharmacy involvement here, which hopefully it's going to start and that's a great thing you know it improves our prescribing overall.'* **Site 4, interview 3 (Consultant)**
2. Memory/attention and decision processes **Behaviour change wheel interventions identified:** **-Enablement** **-Modelling**	*'You know sometimes you're writing three or four pages of a drug kardex, and to look at every possible interaction, you know you'd see the common things but the less common things get overlooked all the time.'* **Site 2, interview 3 (SHO)** *'. . . some people just believe everything the patient says at face value without ever really investigating whether or not they actually know what they are talking about'* **Site 4, interview 1 (SHO)** *'I think you have to be more thoughtful prescribing for elderly patients and I think a lot of people just do it without taking enough care and stuff like that, you know you have to know what you're prescribing and you do have to be aware of any interactions.'* **Site 3, interview 2 (Consultant)**
3 and 4. Knowledge and skills **Behaviour change wheel interventions identified:** **-Enablement** **-Modelling**	*'It's a different knowledge set. And it's difficult you know because there isn't a huge amount of data out there, or its not communicated to us very well, I mean we all hear about the randomized controlled trials when new drugs come out, we get info* [information] *about that but we don't really hear much like, on grand rounds you know, what meds are good or bad in elderly people'* **Site 1, interview 5 (Reg)** *'. . . as an undergrad, students don't have a tenth of the teaching that they should have, all doctors of all levels will openly put their hand up and say, as an undergrad, they didn't have the teaching so most definitely there should be an increase in what they are teaching in clinical pharmacy, they should have a huge amount more time at undergraduate level for that because it's such a dangerous occupation you know, prescribing, something has to be done about it ya'* **Site 3, interview 1 (Intern)** *'I think we do need a lot more patient education, I think we do need the patients, not only going home, not only having a prescription, but they have a detailed patient education leaflet, documenting all the drugs they are on, and their purpose, frequency and duration.'* **Site 2, interview 1 (Consultant)**
5. Social influences **Behaviour change wheel interventions identified:** **-Restrictions** **-Persuasion**	*'there is no doubt that we would come under pressure to prescribe anti- depressants or sleeping tablets from the family members, not just the person and you have to resist that if you think it is inappropriate but you know, the fact that you have to resist it means that sometimes you probably are swayed by it. And similarly there may be a medication that you may be thinking of prescribing and the family say absolutely no, or have huge concerns about it you know if you are iffy about it, that might be enough to dissuade you.'* **Site 3, interview 2 (Consultant)** *'I'd start with education actually, but its educating patients as well you know. There's a notion out there you know that you go to the doctor, and the outcome of any consultation should be a prescription.'* **Site 4, interview 4 (Consultant)**

which advice from pharmacists was communicated to the prescribers was important, with interviewees favouring face-to-face communication rather than written communication.

'. . . obviously it would be nice to think that every ward would have a pharmacist attached to it reviewing kardexes [prescription charts] and educating (. . . .) but there is a feeling that the pharmacist

comes and writes a note for you, but it's not done face to face, and it actually is a bit antagonistic if anything (. . . .) having post-its [notes] stuck on things saying please review this, please review that, we all hate notes, everyone hates it, so I think that could be done better. So more pharmacy input, but more integrated pharmacy input' **Site 3, interview 2 (Consultant)**

Memory/attention and decision processes Participants referred to this domain in two contexts. Firstly, in conjunction with the high pressure environment in which they prescribe and their workload. This environment affects the attention they can give to each patient and their medicines. Their attention is not at the level it would otherwise be.

'Particularly in A&E (accident and emergency) which is where you are doing the core prescribing, trying to determine what they should be on., making decisions about whether to hold things or not, and I mean there are four SHOs (senior house officers) trying to talk you, along with nurses and stuff' **Site 1, interview 1 (Registrar)**

Secondly, several participants suggested doctors' decision-making and the processes surrounding it as a cause of PIP. There was a feeling amongst these participants that there was wide variation in practice amongst doctors, and that some did not go to the lengths required to make an informed decision when prescribing.

'. . . when they come in, and they don't have a list of their medications, some people inappropriately just write down the dose that they think that they should be on or whatever, which often commonly happens, or a prescription of a patient that just came in on Sunday, had just the medications written with no doses at all (. . . .) so if you're not going to write a dose you probably shouldn't write anything.' **Site 1, interview 1 (Registrar)**

Knowledge/Skills Although separated into two domains in the TDF, participants for the most part eluded to constructs within these domains as a single domain, and thus, we have reported these together. Participants noted a lack of specific education and training in geriatric pharmacotherapy, and also a lack of communication of clinically relevant information with regards to older patients, for example, which drugs to avoid. Interviewees noted that experiential learning is how their prescribing skills and knowledge of issues around prescribing in older people progress. However they felt that this was not sufficient and that further structured training was required.

'I'd say if there was a kind of a monthly, or periodic review of the literature (. . .) to kind of put out a newsletter or something, for medications that are found to be obsolete, medications that are found to be harmful, because we see a lot of people on medication that were used 10 or 20 years ago and are no longer in the guidelines and no longer the current practice (. . .) I think that would be a good idea.' **Site 2, interview 2 (Registrar)**

'I don't think there is enough training for prescribing in older patients. There is no distinction between older patients and the general adult population in the training. You just learn it from practice.' **Site 4, interview 2 (Registrar)**

Patient education was also considered important.

'And even when they bring a list, their knowledge of those meds is not good. And the patient education of his/her own drug therapies is fairly poor. Community wise, nationwide, there is a big area that needs to be addressed in terms of patient education' **Site 2, interview 1 (Consultant)**

Social influences Participants were specifically asked about outside influences that may affect their prescribing and perhaps increase the risk of PIP. The majority of doctors admitted that patients and/or patients' families can influence their prescribing, to the point where the doctor prescribes something he/she is not totally happy with.

'you as a doctor sometimes have, you feel that you have to do something, you get pressurized by either nursing staff, relatives or patients. You have to give them something. So you end up giving something that you are not 100% happy with.' **Site 2, interview 2 (Registrar)**

They did however say that they did not think these choices were putting their patients at any risk due to these choices after weighing the risks and benefits and that the quality of life was a major deciding factor.

'I would like to think that we never prescribe something that we know is wrong or don't prescribe something that we know is right, even if the family has concerns, I do think we can stand our ground and document their concerns and do it (. . .) I think we are always just thinking about the patient's quality of life (. . .) but there's no doubt it sways you where it's a grey area' **Site 3, interview 2 (Consultant)**

Barriers to behaviour change

From the above analysis, it can be seen that the main barriers to appropriate prescribing are:

- An environment which is conducive to sub-optimal prescribing
  - Interruptions, lack of IT infrastructure, chaotic surroundings, all combine making it very difficult for the prescriber to give the extra thought required to ensure the older patient's prescription is appropriate.
- Strained resources
  - Lack of targeted pharmacy input on the wards, poor collaboration between different levels of care due to busy schedules and, again, lack of IT infrastructure.
- Lack of specific training
  - Not enough geriatric pharmacotherapy training, particularly for undergraduates. Prescribers feel ill-equipped to prescribe appropriately.
- Poor patient education
  - Patients' knowledge of their own medicines is generally poor and they can often be reluctant to change. This can make adjusting medications difficult for the prescriber.

Behaviour change wheel

Having identified the domains within the TDF [20] that are relevant to PIP, we then used the behaviour change wheel [31] to identify intervention types that would be suitable to address these domains. According to the behaviour change wheel, the types of interventions that would be beneficial in the area of PIP are training, environmental restructuring, restrictions, persuasion, incentivization, modelling and enablement.

Discussion

This is the first study to use a theoretical approach to investigate issues associated with PIP, with interesting findings.

The responses to the general questions at the start of the interviews paint a clear picture. Doctors are aware that PIP is problematic in this age group. Their estimations of its prevalence were quite accurate. However they feel ill-equipped to deal with it and are ill-informed about the measures that already exist to deal with it, illustrated by their widespread lack of awareness of the common screening tools for prescribing in older patients.

The consensus amongst all doctors (not just those in geriatrics) that increased exposure to geriatricians would be of great benefit is an important point. Of course it makes sense that guidance from experienced geriatricians would improve prescribing in older patients, but to hear it from doctors on the ground, who have experienced prescribing within multiple specialities emphasizes this point. It is also of interest that the same TDF domains were identified from the transcripts of doctors working in geriatrics and those not in geriatrics. This is not surprising, however, as doctors from all medical specialties are seeing more and more older patients now and so the challenges to prescribing for these patients are clear to all.

The domains in the TDF identified as relevant provide the details to the picture painted above. It is a well-known fact that a doctor's workplace can be chaotic [33, 34], and so the emergence of 'environmental context and resources' was not unexpected. Improving the environment in which doctors prescribe is not an easy task. However, areas have been highlighted throughout these interviews that could be good starting points, for example, making better use of the resources available, in particular, the hospital pharmacist, perhaps interventions designed to restrict interruptions to doctors while writing prescriptions, or, thinking bigger, improved IT infrastructure would undoubtedly improve prescribing across the board.

The domain of 'memory/attention and decision processes' was strongly intertwined with the domain of 8'environmental context and resources'. In an ideal world, with a calm environment and no distractions, prescribing is still a challenging exercise. The complexity of prescribing is well documented. Aronson has identified the need for a wide range of skills and judgment when prescribing, and the increased difficulties when dealing with a vulnerable population [35–37]. Add in the extra stresses the environment brings with it and the exercise becomes significantly more difficult, not only to remember the important information, but to make the right decision. Doctors' indications that decision making processes, particularly when writing prescriptions, vary quite significantly between individuals is a point to consider, and a possible target for intervention. Again, providing an environment more conducive to appropriate prescribing will address this to some extent. However, the interviews also suggest that, perhaps, greater care to standardize doctors' practise should be taken.

'Knowledge' and 'skills' were two clear areas participants felt could be targeted, although for the most part they referred to these domains as one. The majority of interviewees expressed a desire for further training. Those who did not were the most senior doctors i.e. hospital consultants. Not only do they feel they do not receive adequate *specific* geriatric pharmacotherapy training as medical students, but also, there is a perceived lack of communication of the salient points from modern literature and research once they qualify. This, we feel, is the area with the most potential for intervention in terms of feasibility. Pharmacists and clinical pharmacologists are ideally placed to address this issue and equip doctors with the necessary tools to prescribe for older patients. A change in the undergraduate curriculum is also clearly needed, with more emphasis on geriatric pharmacotherapy.

The most unexpected result of the study was the emergence of the domain 'social influences'. Over half the participants, including the majority of consultants, said that they would be, and/or have been influenced by the patient or their family to prescribe in a manner that could be deemed inappropriate, with several doctors using the term '*forced to prescribe*'. Although most added that they still felt they were not putting the patient at risk, this idea of a doctor feeling forced into a decision is worrying. This correlates well with a recent meta-synthesis on PIP, which found that some doctors feel restricted in terms of their abilities to prescribe appropriately due to a combination of factors such as pressure to please the patients and fear of doing harm by changing a patient's medications [38]. Many of them referred to patient education as a solution to this. The area of shared decision making [39] should also be explored as a means to address this issue that doctors have identified as problematic. This would also counteract the traditional paternalistic approach to prescribing which has previously been identified as problematic and contributory to PIP [40]. However, it should also be noted that while doctors admitted to sometimes knowingly prescribing inappropriately, in certain circumstances, they were conscious of paying more heed to the patients' quality of life rather than the appropriateness of their prescription. This is an important consideration as these patients' requirements can be very different from the average adults.

This study has highlighted the specific barriers to change that exist in the area of PIP. The intervention functions identified through use of the behaviour change wheel correlate well with these barriers, in that, interventions based on environmental restructuring and training would certainly seem logical given that three of the four barriers identified fall under 'environment' or 'training'. We can be confident, therefore, that an intervention informed by these techniques would be justified and beneficial.

To date, interventions that reliably counteract PIP in older patients are lacking. O'Connor *et al*. [41] recently conducted a review which suggests four areas of intervention to counteract PIP in this population, namely comprehensive geriatric assessment, medication use review, prescriber education/audit/feedback and computerized prescriber order entry with clinical decision support. The evidence to support any of these interventions to prevent PIP in older patients is weak. Prescriber education interventions to prevent PIP in particular drug classes have been shown to work, e.g. antibiotics, opioid analgesics and antipsychotics [41]. Although the TDF domains were examined and presented individually, there is significant crossover between them. The environmental context of course has an impact on doctors' memory/attention and decision processes, as well as their ability to carry out basic skills. Similarly, a doctors' particular skill set may determine whether or not they are prone to social influences and whether they allow such pressures to impact on their prescribing. Bearing these crossovers between domains in mind, it is certain that an intervention to address PIP will have to be multifaceted. One of the intervention types identified by the behaviour change wheel is unlikely to result in a significant improvement. A combination of intervention types however would be well justified and, in the authors' opinions, have a high chance of success.

Limitations

Recruitment of participants for this study was largely the responsibility of a third party i.e. the hospital pharmacist. While it served well to have a person known to the medical staff introduce the project, it is preferable that the researcher(s) claim responsibility for recruitment when using qualitative methodologies.

Whilst the sampling matrix was conducted to ensure inclusivity within the hospital setting, this study therefore reflects the barriers encountered by hospital doctors, and is not generalizable to primary care.

The sample size of 22, although acceptable for qualitative research, is small, and as with all qualitative research, the results are therefore not generalizable.

In conclusion, doctors are quite aware that PIP in older patients is a real problem that needs addressing. It seems the causes are a combination of environmental and social factors, compounded by doctors' lack of specific training and education in geriatric pharmacotherapy. This study has identified key areas for targeting of intervention studies in the future, as well as intervention types that should be used.

Competing Interests

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare SC had grant funding from the Health Research Board of Ireland to cover expenses to deliver a lecture at the European Society of Clinical Pharmacy (ESCP) conference 2013. There are no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

The authors would like to acknowledge the staff of each of the hospitals who took part in this study, particularly the chief pharmacists for their support and assistance.

The authors would also like to acknowledge the Health Research Board of Ireland (HRB) for funding this research. Grant number HRA_HSR/2010/14.

REFERENCES

1 Kinsella K, Wan H. An aging world: 2008. 2009.

2 Cherubini A, Corsonello A, Lattanzio F. Underprescription of beneficial medicines in older people: causes, consequences and prevention. Drugs Aging 2012; 29: 463–75.

3 Steinman MA, Landefeld CS, Rosenthal GE, Berthenthal D, Sen S, Kaboli PJ. Polypharmacy and prescribing quality in older people. J Am Geriatr Soc 2006; 54: 1516–23.

4 Gallagher P, Barry P, O'Mahony D. Inappropriate prescribing in the elderly. J Clin Pharm Ther 2007; 32: 113–21.

5 Gupta S, Rappaport HM, Bennett LT. Inappropriate drug prescribing and related outcomes for elderly medicaid beneficiaries residing in nursing homes. Clin Ther 1996; 18: 183–96.

6 Rancourt C, Moisan J, Baillargeon L, Verreault R, Laurin D, Gregoire JP. Potentially inappropriate prescriptions for older patients in long-term care. BMC Geriatr 2004; 4: 9–18.

7 Ryan C, O'Mahony D, Kennedy J, Weedle P, Byrne S. Potentially inappropriate prescribing in an Irish elderly population in primary care. Br J Clin Pharmacol 2009; 68: 936–47.

8 Dunn RL, Harrison D, Ripley TL. The beers criteria as an outpatient screening tool for potentially inappropriate medications. Consult Pharm 2011; 26: 754–63.

9 Spiker EC, Emptage RE, Giannamore MR, Pedersen CA. Potential adverse drug events in an indigent and homeless geriatric population. Ann Pharmacother 2001; 35: 1166–72.

10 Gallagher P, Lang PO, Cherubini A, Topinkova E, Cruz-Jentoft A, Montero Errasquin B, Madlova P, Gasperini B, Baeyens H, Baeyens JP, Michel JP, O'Mahony D. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. Eur J Clin Pharmacol 2011; 67: 1175–88.

11 O'Sullivan DP, O'Mahony D, Parsons C, Hughes C, Murphy K, Patterson S, Byrne S. A prevalence study of potentially inappropriate prescribing in Irish long-term care residents. Drugs Aging 2013; 30: 39–49.

12 Damestoy N, Collin J, Lalande R. Prescribing psychotropic medication for elderly patients: some physicians' perspectives. CMAJ 1999; 161: 143–5.

13 Cook JM, Marshall R, Masci C, Coyne JC. Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study. J Gen Intern Med 2007; 22: 303–7.

14 Agarwal G, Nair K, Cosby J, Dolovich L, Levine M, Kaczorowski J, Butler C, Burns S. GPs' approach to insulin prescribing in older patients: a qualitative study. Br J Gen Pract 2008; 58: 569–75.

15 Wood-Mitchell A, James IA, Waterworth A, Swann A, Ballard C. Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study. Age Ageing 2008; 37: 547–52.

16 Dickinson R, Knapp P, Dimri V, Holmes J, House A, Petty D, Raynor DK, Zermansky A. The long-term use of antidepressants in the older population: a qualitative study. Int J Pharm Pract 2009; 17 (S2): 26–52.

17 Spitz A, Moore AA, Papaleontiou M, Granieri E, Turner BJ, Reid MC. Primary care providers' perspective on prescribing opioids to older adults with chronic non-cancer pain: a qualitative study. BMC Geriatr 2011; 11: 35.

18 Albarracin D, Gillette JC, Earl AN, Glasman LR, Durantini MR, Ho MH. A test of major assumptions about behavior change: a comprehensive look at the effects of passive and active HIV-prevention interventions since the beginning of the epidemic. Psychol Bull 2005; 131: 856–97.

19 Noar SM, Zimmerman RS. Health behavior theory and cumulative knowledge regarding health behaviors: are we moving in the right direction? Health Educ Res 2005; 20: 275–90.

20 Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A. Making psychological theory useful for implementing evidence based practice: a consensus approach. Qual Saf Health Care 2005; 14: 26–33.

21 Duncan EM, Francis JJ, Johnston M, Davey P, Maxwell S, McKay GA, Mclay J, Ross S, Ryan C, Webb DJ, Bond C. Learning curves, taking instructions, and patient safety: using a theoretical domains framework in an interview study to investigate prescribing errors among trainee doctors. Implement Sci 2012; 7: 86–95.

22 Michie S, Johnston M, Francis J, Hardeman W, Eccles M. From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques. Appl Psychol 2008; 57: 660–80.

23 Pitt VJ, O'Connor D, Green S. Referral of people with osteoarthritis to self-management programmes: barriers and enablers identified by general practitioners. Disabil Rehabil 2008; 30: 1938–46.

24 Amemori M, Michie S, Korhonen T, Murtomaa H, Kinnunen TH. Assessing implementation difficulties in tobacco use prevention and cessation counselling among dental providers. Implement Sci 2011; 6: 50–9.

25 Ritchie J, Lewis J. Qualitative Research Practice a Guide for Social Science Students and Researchers. London: Sage publications, 2008.

26 Dyson J, Lawton R, Jackson C, Cheater F. Does the use of a theoretical approach tell us more about hand hygiene behaviour? The barriers and levers to hand hygiene. J Infect Prev 2011; 12: 17–24.

27 Ritchie J, Spencer L. Qualitative Data Analysis for Applied Policy Research. Bryman A, Burgess R, editor. London: Routledge, 1994.

28 Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res 2005; 15: 1277–88.

29 Carey JW, Morgan M, Oxtoby MJ. Intercoder agreement in analysis of responses to open-ended interview questions: examples from tuberculosis research. Field Methods 1996; 8: 1–5.

30 Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. Implement Sci 2012; 7: 37–46.

31 Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implement Sci 2011; 6: 42–52.

32 Francis JJ, Johnston M, Robertson C, Glidewell L, Entwistle V, Eccles MP, Grimshaw JM. What is an adequate sample size? Operationalising data saturation for theory-based interview studies. Psychol Health 2010; 25: 1229–45.

33 Dean B, Schachter M, Vincent C, Barber N. Causes of prescribing errors in hospital inpatients: a prospective study. Lancet 2002; 359: 1373–8.

34 Coombes ID, Stowasser DA, Coombes JA, Mitchell C. Why do interns make prescribing errors? A qualitative study. Med J Aust 2008; 188: 89–94.

35 Aronson JK. Balanced prescribing – principles and challenges. Br J Clin Pharmacol 2012; 74: 566–72.

36 Aronson JK, Barnett DB, Ferner RE, Ferro A, Henderson G, Maxwell SR, Rawlins MD, Webb DJ. Poor prescribing is continual. BMJ 2006; 333: 756–68.

37 Aronson JK, Henderson G, Webb DJ, Rawlins MD. A prescription for better prescribing. BMJ 2006; 333: 459–60.

38 Cullinan S, O'Mahony D, Fleming A, Byrne S. A meta-synthesis of potentially inappropriate prescribing in older patients. Drugs Aging 2014; 31: 631–8.

39 Davis RE, Dolan G, Thomas S, Atwell C, Mead D, Nehammer S, Moseley L, Edwards A, Elwyn G. Exploring doctor and patient views about risk communication and shared decision-making in the consultation. Health Expect 2003; 6: 198–207.

40 Spinewine A, Swine C, Dhillon S, Franklin BD, Tulkens PM, Wilmotte L, Lorant V. Appropriateness of use of medicines in elderly inpatients: qualitative study. Br Med J 2005; 331: 935–8.

41 O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. Drugs Aging 2012; 29: 437–52.

11.5 Appendix V: Theoretical domains framework

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Table 1 Theoretical domains, component constructs, and eliciting questions for investigating the implementation of evidence-based practice

Domains*	Constructs	Interview questions
(1) Knowledge	Knowledge Knowledge about condition/scientific rationale Schemas+mindsets+illness representations Procedural knowledge	Do they know about the guideline? What do they think the guideline says? What do they think the evidence is? Do they know they should be doing *x*? Do they know why they should be doing *x*?
(2) Skills (Skills)	Skills Competence/ability/skill assessment Practice/skills development Interpersonal skills Coping strategies	Do they know how to do *x*? How easy or difficult do they find performing *x* to the required standard in the required context?
(3) Social/professional role and identity (Self-standards)	Identity Professional identity/boundaries/role Group/social identity Social/group norms Alienation/organisational commitment	What is the purpose of the guidelines? What do they think about the credibility of the source? Do they think guidelines should determine their behaviour? Is doing *x* compatible or in conflict with professional standards/identity? (prompts: moral/ethical issues, limits to autonomy) Would this be true for all professional groups involved?
(4) Beliefs about capabilities (Self-efficacy)	Self-efficacy Control—of behaviour and material and social environment Perceived competence Self-confidence/professional confidence Empowerment Self-esteem Perceived behavioural control Optimism/pessimism	How difficult or easy is it for them to do *x*? (prompt re. internal and external capabilities/constraints) What problems have they encountered? What would help them? How confident are they that they can do *x* despite the difficulties? How capable are they of maintaining *x*? How well equipped/comfortable do they feel to do *x*?
(5) Beliefs about consequences (Anticipated outcomes/attitude)	Outcome expectancies Anticipated regret Appraisal/evaluation/review Consequents Attitudes Contingencies Reinforcement/punishment/consequences Incentives/rewards Beliefs Unrealistic optimism Salient events/sensitisation/critical incidents Characteristics of outcome expectancies–physical, social, emotional; Sanctions/rewards, proximal/distal, valued/not valued, probable/improbable, salient/not salient, perceived risk/threat	What do they think will happen if they do *x*? (prompt re themselves, patients, colleagues and the organisation; positive and negative, short term and long term consequences) What are the costs of *x* and what are the costs of the consequences of *x*? What do they think will happen if they do not do *x*? (prompts) Do benefits of doing *x* outweigh the costs? How will they feel if they do/don't do *x*? (prompts) Does the evidence suggest that doing *x* is a good thing?
(6) Motivation and goals (Intention)	Intention; stability of intention/certainty of intention Goals (autonomous, controlled) Goal target/setting Goal priority Intrinsic motivation Commitment Distal and proximal goals Transtheoretical model and stages of change	How much do they want to do *x*? How much do they feel they need to do *x*? Are there other things they want to do or achieve that might interfere with *x*? Does the guideline conflict with others? Are there incentives to do *x*?
(7) Memory, attention and decision processes	Memory Attention Attention control Decision making	Is *x* something they usually do? Will they think to do *x*? How much attention will they have to pay to do *x*? Will they remember to do *x*? How? Might they decide not to do *x*? Why? (prompt: competing tasks, time constraints)
(8) Environmental context and resources (Environmental constraints)	Resources/material resources (availability and management) Environmental stressors Person × environment interaction Knowledge of task environment	To what extent do physical or resource factors facilitate or hinder *x*? Are there competing tasks and time constraints? Are the necessary resources available to those expected to undertake *x*?
(9) Social influences (Norms)	Social support Social/group norms Organisational development Leadership Team working Group conformity Organisational climate/culture Social pressure Power/hierarchy Professional boundaries/roles Management commitment Supervision Inter-group conflict Champions Social comparisons Identity; group/social identity Organisational commitment/alienation Feedback Conflict—competing demands, conflicting roles	To what extent do social influences facilitate or hinder *x*? (prompts: peers, managers, other professional groups, patients, relatives) Will they observe others doing *x* (i.e. have role models)?

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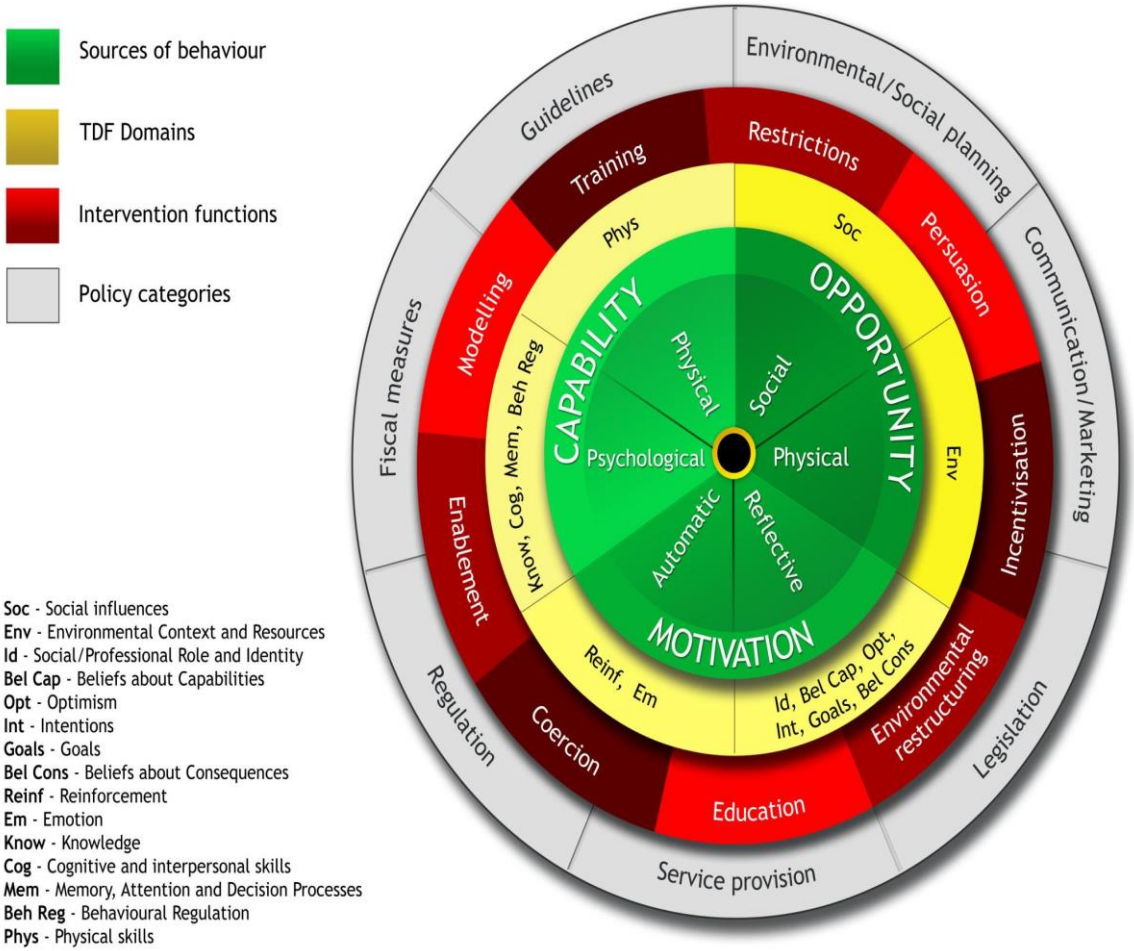
Table 1 Continued

Domains*	Constructs	Interview questions
	Change management Crew resource management Negotiation Social support: personal/professional/organisational, intra/interpersonal, society/community Social/group norms: subjective, descriptive, injunctive norms Learning and modelling	
(10) Emotion (Emotion)	Affect Stress Anticipated regret Fear Burn-out Cognitive overload/tiredness Threat Positive/negative affect Anxiety/depression	Does doing *x* evoke an emotional response? If so, what? To what extent do emotional factors facilitate or hinder *x*? How does emotion affect *x*?
(11) Behavioural regulation	Goal/target setting Implementation intention Action planning Self-monitoring Goal priority Generating alternatives Feedback Moderators of intention-behaviour gap Project management Barriers and facilitators	What preparatory steps are needed to do *x*? (prompt re individual and organisational) Are there procedures or ways of working that encourage *x*?
(12) Nature of the behaviours	Routine/automatic/habit Breaking habit Direct experience/past behaviour Representation of tasks Stages of change model	What is the proposed behaviour (x)? Who needs to do what differently when, where, how, how often and with whom? How do they know whether the behaviour has happened? What do they currently do? Is this a new behaviour or an existing behaviour that needs to become a habit? Can the context be used to prompt the new behaviour? (prompts: layout, reminders, equipment) How long are changes going to take? Are there systems for maintaining long term change?

*Corresponding constructs from Fishbein *et al*[6] shown in parentheses.

11.6 Appendix VI: Behaviour change wheel

(Reproduced with permission, September 2015, Prof. Susan Michie)



Soc - Social influences
Env - Environmental Context and Resources
Id - Social/Professional Role and Identity
Bel Cap - Beliefs about Capabilities
Opt - Optimism
Int - Intentions
Goals - Goals
Bel Cons - Beliefs about Consequences
Reinf - Reinforcement
Em - Emotion
Know - Knowledge
Cog - Cognitive and interpersonal skills
Mem - Memory, Attention and Decision Processes
Beh Reg - Behavioural Regulation
Phys - Physical skills

The domains of the TDF are presented in yellow here. Depending on which domains are identified, they can be mapped to the suitable intervention types, shown here in red.

11.7 Appendix VII: Interview Topic Guide

"Before we start I just want to check that you're still happy for this interview to be recorded and that you know we can stop at any time?

I'd like to thank you for agreeing to participate in this interview and stress that everything said here today is completely confidential. Your name will not appear on any documents or recording discs and I personally will anonymise the transcript from this interview, and will ensure that no one else will be identifiable either.

There won't be any consequences to what you tell me and there will be no blame attributed to you or anyone else.

These interviews are part of my PhD which is looking at inappropriate prescribing in older patients and the processes that surround it. Inappropriate Prescribing for older people, and by older I mean over the age of 65, is an important cause of adverse events in hospitals and by investigating how this happens, we hope we can develop further studies aimed at improving prescribing for older people.

There are no right or no wrong answers to these questions, just give as much detail as you can. It will probably last about 30 minutes.

Does all that sound ok? Are you happy for me to record the interview?

Demographic Questions:

- Physicians' Grade:
- Gender:
- How many years have you worked as a doctor?
- Are you currently working in any particular speciality?
    - What specialities have you experienced?
- Do you have any specific training in geriatric medicine?
    - Undergrad/postgrad?
- Where did you complete your undergraduate training?

(Prompts are in red)

1. Could you tell me what you understand by the term *" INAPPROPRIATE PRESCRIBING"*?
    - Can you give an example?
    - Drug with wrong/no indication?
    - Drug with high risk of ADR
    - Drug that is unnecessarily expensive?
    - Prescribed for too short or too long a period?
    - Failure to prescribe a drug for irrational or ageist reasons?

A number of studies have looked at prescribing in older patients, and have tried to estimate how much of it is inappropriate.

2. What proportion of *OLDER PEOPLE* i.e. ≥65 years, would you say are prescribed at least one inappropriate medicine?

    A. Upon admission
    B. During their stay in hospital
    C. On discharge

    Do you think the level of inappropriate prescribing is a problem in amongst older patients?

    - Primary care?
    - Secondary care?
    - Tertiary care?

3. What do you think contributes to inappropriate prescribing in older people?

    Age, major polypharmacy, comorbidities (eg heart failure, renal impairment, hepatic impairment), multiple doctors, hx of falls?

4. Do you think there is anything in particular you should know more about when you are prescribing for older people?

    Clinical knowledge

    Procedural knowledge

5. Could you tell me what you understand by the term adverse drug reaction?

What classes of drug would you say are likely to be problematic in older patients?
What percentage of older patients would you say experience an adverse drug reaction?

6. On a scale of 1 to 10, how would you rate your confidence in prescribing for older people, 1 being not confident at all and 10 being very confident?

   Compared to prescribing for the general adult population?
   Is it a different skill?

   What parts of the prescribing process would you be least confident about?

   Deciding on the drug, appropriateness of drug, dose, duration?

7. What would you say the potential consequences of inappropriate prescribing are?

   For: Patient, you, job, colleagues, patient's family, etc

8. Do you think the possibility of prescribing an inappropriate medicine is something that is on doctors' minds on a day to day basis?

9. As a (*grade and speciality of doctor here*) doctor, how would you describe your own role in ensuring medicines prescribed for older people are appropriate?

   Directly involved?
   Not much input?
   Reviewing charts.

10. Would you feel comfortable changing an inappropriate prescription if it was highlighted to you, if not, why not?

    If you had prescribed something and it was highlighted to you?
    If you noticed something else someone had prescribed?
    Have you done it in the past?
    What would warrant you changing a prescription?

11. From your experience would you say environmental context impact a doctors' prescribing? And does this increase the chance of inappropriate prescribing?

    Time constraints.
    Other tasks.
    Are the necessary resources available?

12. To what extent do the views/actions of your colleagues affect your prescribing?

    Same for patients and patients' families?

13. Do you think your emotions ever impact on prescribing? And does this increase the chance of inappropriate prescribing?

14. Do you think there is a particular way of working or steps that could be taken to encourage appropriate prescribing in older patients?

    Are any of these routinely done at the moment?

15. If something could be done tomorrow to address inappropriate prescribing, what do you think would need to be done differently and who would need to do it?

    Do you think this can be easily achieved?
    What barriers do you see to implementing this?

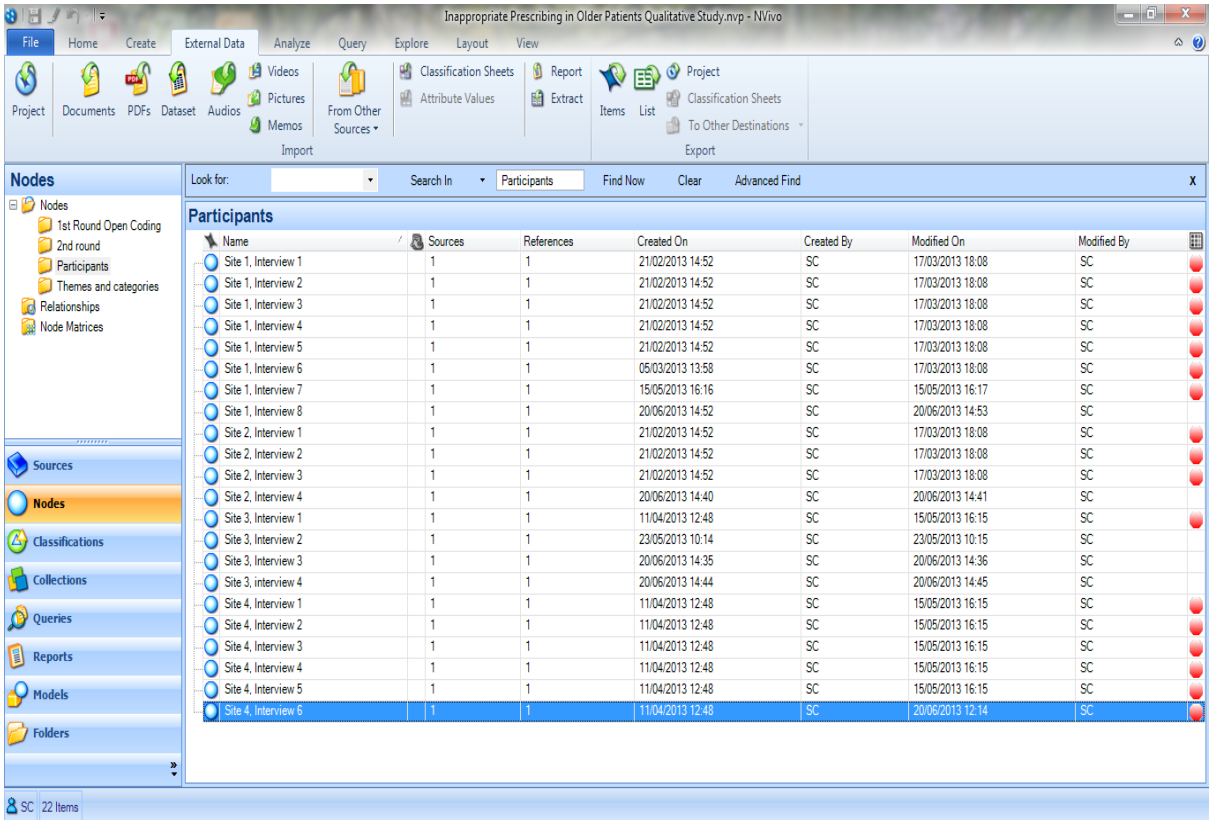
16. What role do you think screening tools play in prescribing for older patients?

    Are you aware of the tools? BEERS, STOPP/START.
    Do you refer to them?

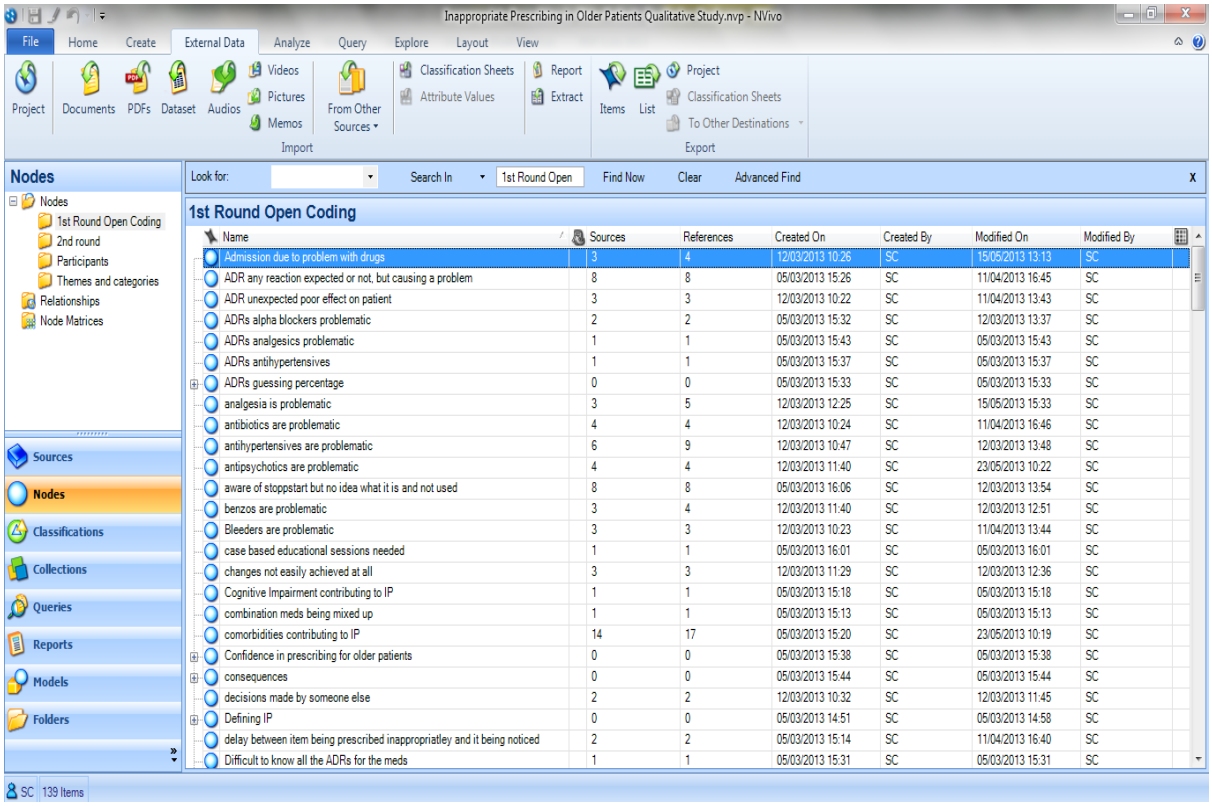
17. Is there anything else you would like to add?

Thank you for your time.

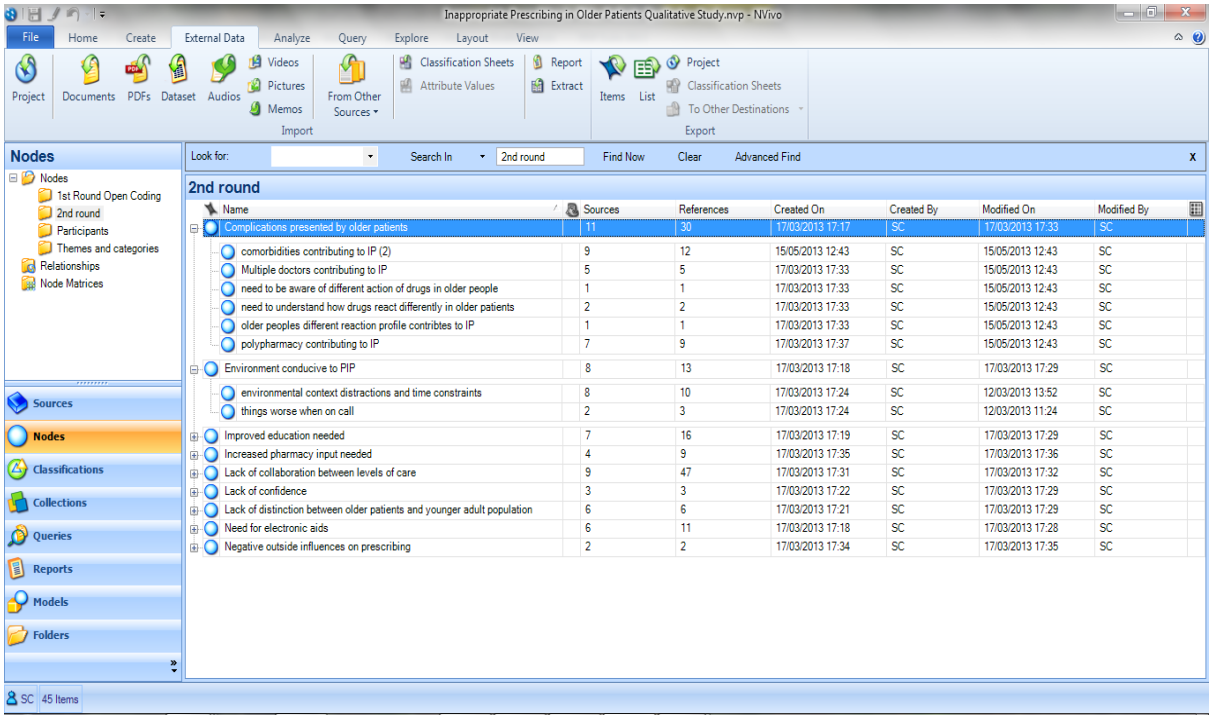
11.8 Appendix VIII: NVivo screen shots of coding process



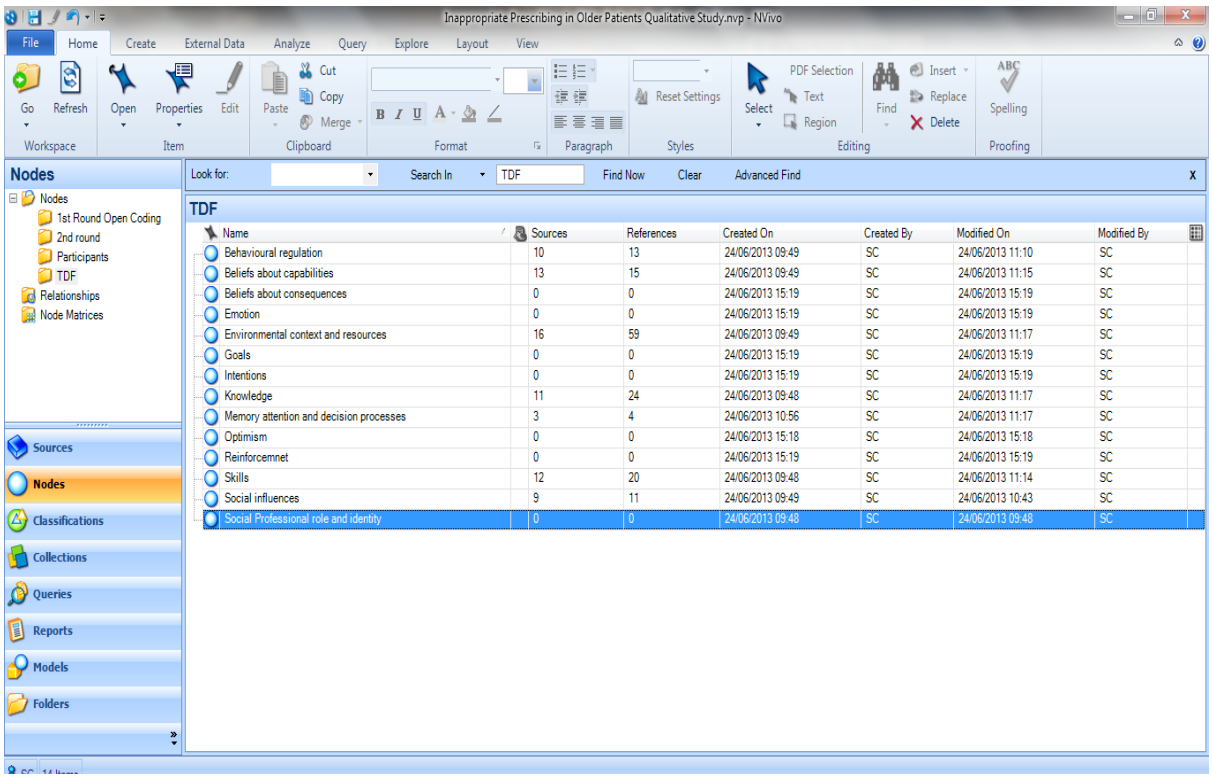
Creation of case nodes



1st round open coding

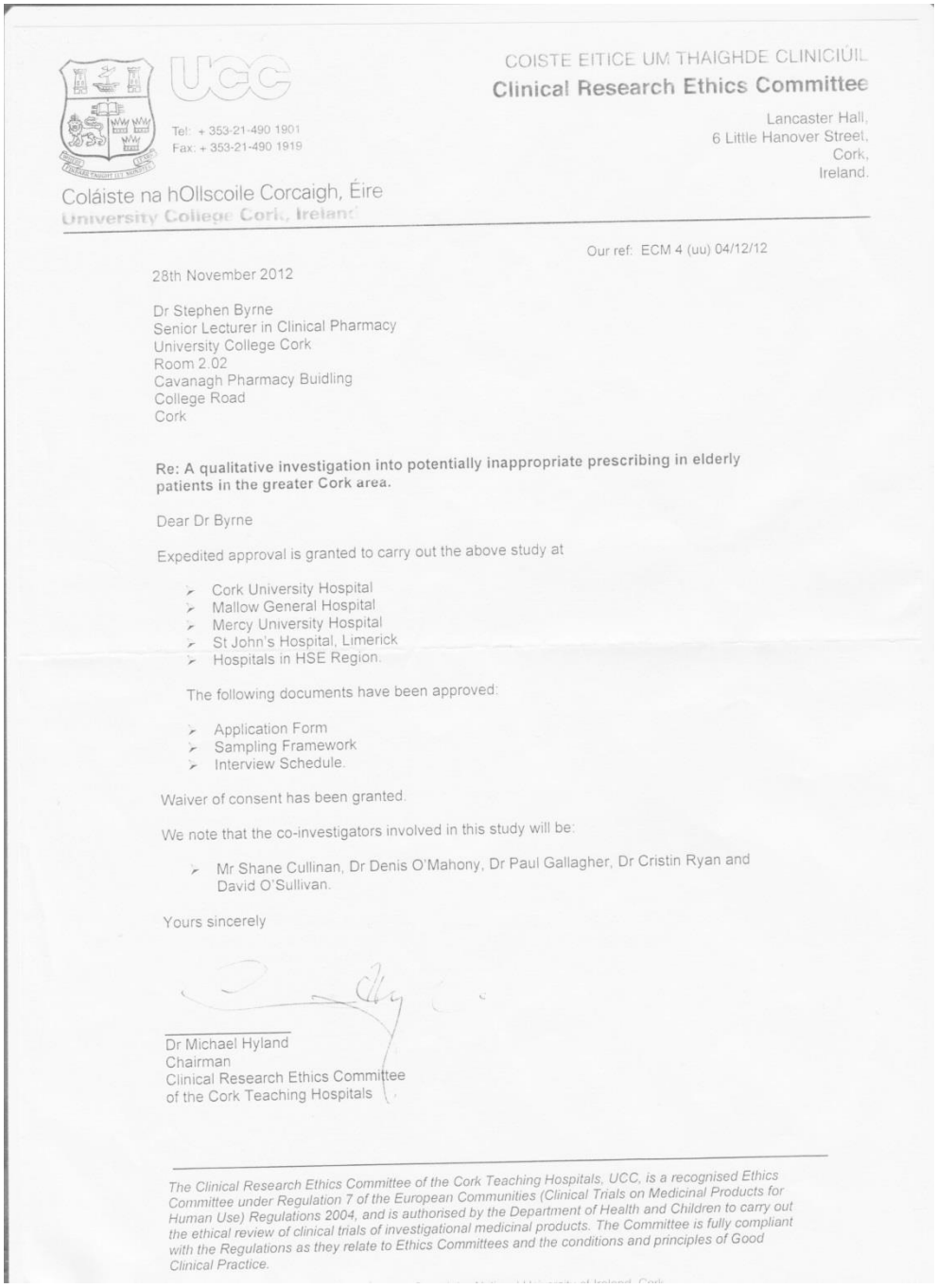


2nd round coding, creation of hierarchies.



Directed content analysis to theoretical domains framework

11.9 Appendix IX: Ethics approval for Chapter 3 research



UCC
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Fax: + 353-21-490 1919
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee
Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (uu) 04/12/12

28th November 2012

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
University College Cork
Room 2.02
Cavanagh Pharmacy Buidling
College Road
Cork

Re: A qualitative investigation into potentially inappropriate prescribing in elderly patients in the greater Cork area.

Dear Dr Byrne

Expedited approval is granted to carry out the above study at

- Cork University Hospital
- Mallow General Hospital
- Mercy University Hospital
- St John's Hospital, Limerick
- Hospitals in HSE Region.

The following documents have been approved:

- Application Form
- Sampling Framework
- Interview Schedule.

Waiver of consent has been granted.

We note that the co-investigators involved in this study will be:

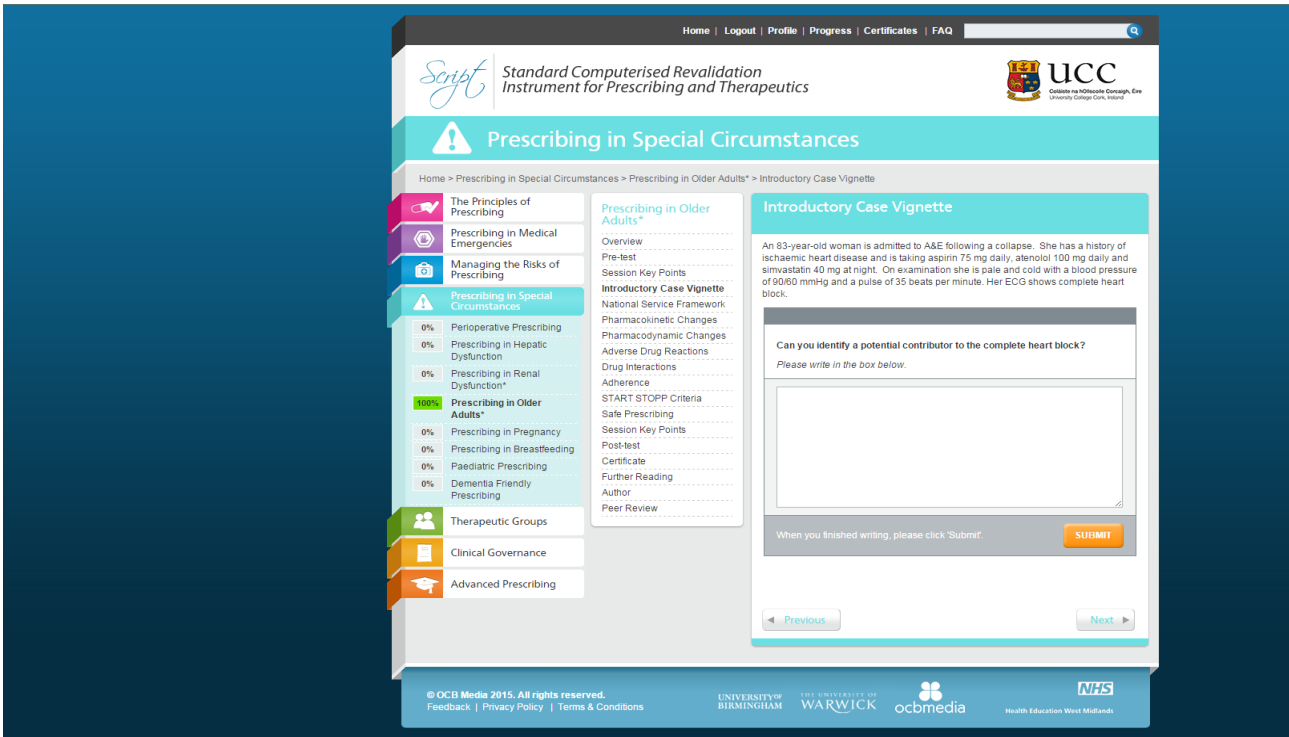
- Mr Shane Cullinan, Dr Denis O'Mahony, Dr Paul Gallagher, Dr Cristin Ryan and David O'Sullivan.

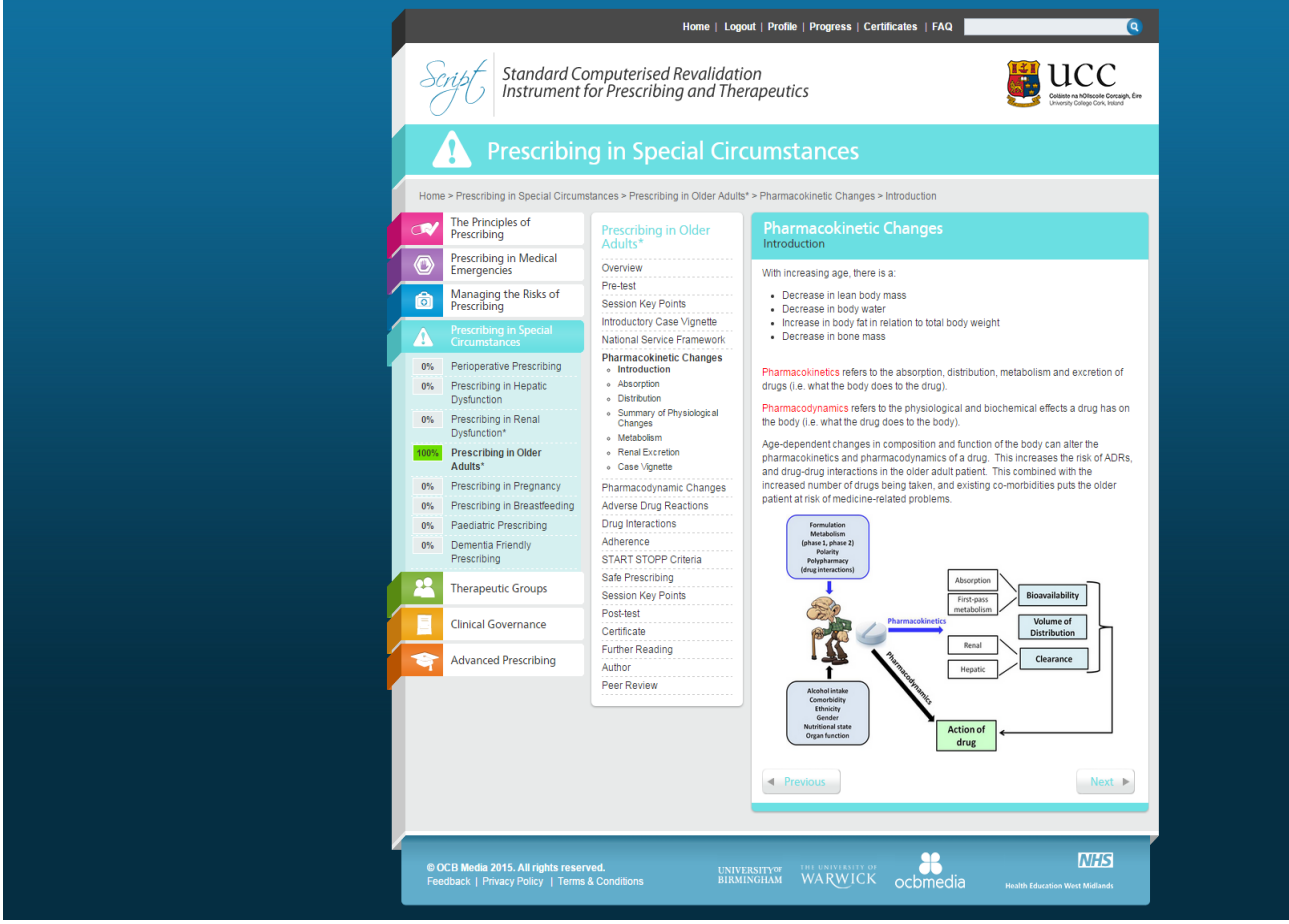
Yours sincerely

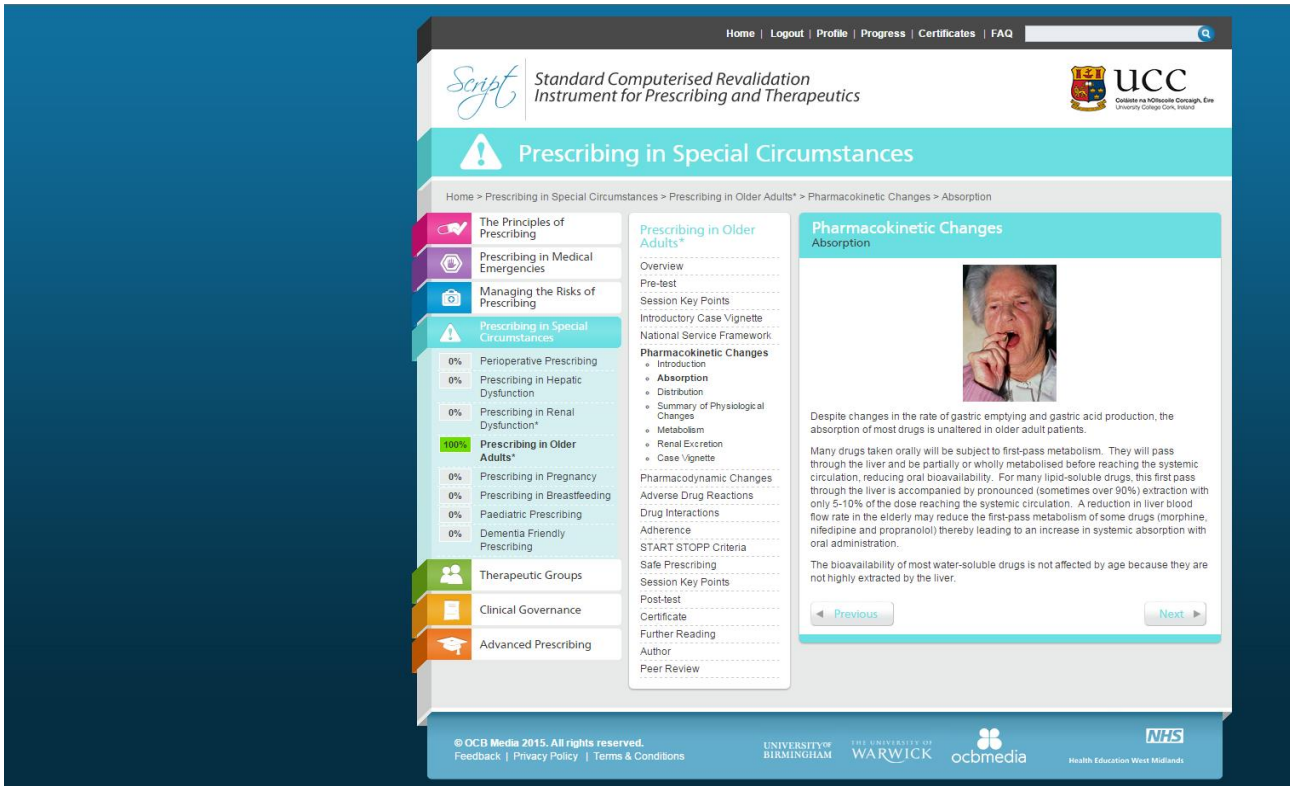
Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

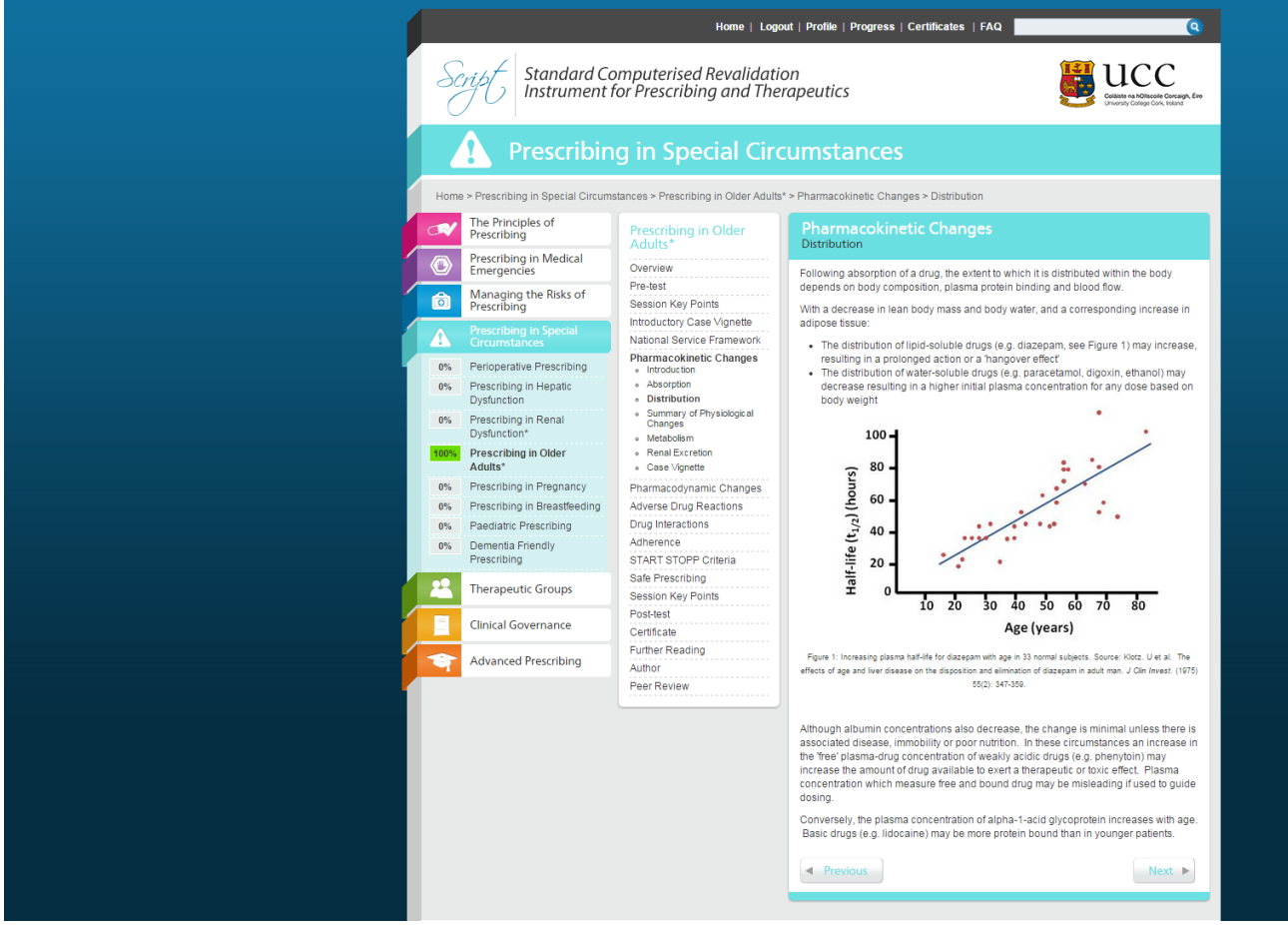
11.10 Appendix X: Screen shots of SCRIPT module






Home | Logout | Profile | Progress | Certificates | FAQ
Script
Standard Computerised Revalidation Instrument for Prescribing and Therapeutics
ucc
Prescribing in Special Circumstances
Home > Prescribing in Special Circumstances > Prescribing in Older Adults* > Pharmacokinetic Changes > Absorption
The Principles of Prescribing
Prescribing in Medical Emergencies
Managing the Risks of Prescribing
Prescribing in Special Circumstances
0% Perioperative Prescribing
0% Prescribing in Hepatic Dysfunction
0% Prescribing in Renal Dysfunction*
100% Prescribing in Older Adults*
0% Prescribing in Pregnancy
0% Prescribing in Breastfeeding
0% Paediatric Prescribing
0% Dementia Friendly Prescribing
Therapeutic Groups
Clinical Governance
Advanced Prescribing
Prescribing in Older Adults*
Overview
Pre-test
Session Key Points
Introductory Case Vignette
National Service Framework
Pharmacokinetic Changes
Introduction
Absorption
Distribution
Summary of Physiological Changes
Metabolism
Renal Excretion
Case Vignette
Pharmacodynamic Changes
Adverse Drug Reactions
Drug Interactions
Adherence
START STOPP Criteria
Safe Prescribing
Session Key Points
Post-test
Certificate
Further Reading
Author
Peer Review
Pharmacokinetic Changes
Absorption
Despite changes in the rate of gastric emptying and gastric acid production, the absorption of most drugs is unaltered in older adult patients.
Many drugs taken orally will be subject to first-pass metabolism. They will pass through the liver and be partially or wholly metabolised before reaching the systemic circulation, reducing oral bioavailability. For many lipid-soluble drugs, this first pass through the liver is accompanied by pronounced (sometimes over 90%) extraction with only 5-10% of the dose reaching the systemic circulation. A reduction in liver blood flow rate in the elderly may reduce the first-pass metabolism of some drugs (morphine, nifedipine and propranolol) thereby leading to an increase in systemic absorption with oral administration.
The bioavailability of most water-soluble drugs is not affected by age because they are not highly extracted by the liver.
Previous
Next
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Script
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Prescribing in Special Circumstances
Home > Prescribing in Special Circumstances > Prescribing in Older Adults* > Pharmacokinetic Changes > Distribution
The Principles of Prescribing
Prescribing in Medical Emergencies
Managing the Risks of Prescribing
Prescribing in Special Circumstances
0% Perioperative Prescribing
0% Prescribing in Hepatic Dysfunction
0% Prescribing in Renal Dysfunction*
100% Prescribing in Older Adults*
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Pharmacodynamic Changes
Adverse Drug Reactions
Drug Interactions
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START STOPP Criteria
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Post-test
Certificate
Further Reading
Author
Peer Review
Pharmacokinetic Changes
Distribution
Following absorption of a drug, the extent to which it is distributed within the body depends on body composition, plasma protein binding and blood flow.
With a decrease in lean body mass and body water, and a corresponding increase in adipose tissue:
The distribution of lipid-soluble drugs (e.g. diazepam, see Figure 1) may increase, resulting in a prolonged action or a 'hangover effect'
The distribution of water-soluble drugs (e.g. paracetamol, digoxin, ethanol) may decrease resulting in a higher initial plasma concentration for any dose based on body weight
Half-life ($t_{1/2}$) (hours)
0
20
40
60
80
100
10 20 30 40 50 60 70 80
Age (years)
Figure 1: Increasing plasma half-life for diazepam with age in 33 normal subjects. Source: Klotz. U et al. The effects of age and liver disease on the disposition and elimination of diazepam in adult man. J Clin Invest. (1975) 55(2): 347-359.
Although albumin concentrations also decrease, the change is minimal unless there is associated disease, immobility or poor nutrition. In these circumstances an increase in the 'free' plasma-drug concentration of weakly acidic drugs (e.g. phenytoin) may increase the amount of drug available to exert a therapeutic or toxic effect. Plasma concentration which measure free and bound drug may be misleading if used to guide dosing.
Conversely, the plasma concentration of alpha-1-acid glycoprotein increases with age. Basic drugs (e.g. lidocaine) may be more protein bound than in younger patients.
Previous
Next

11.11 Appendix XI: Assessments and Marking Schemes for RCT

Baseline assessment

MCQs (20 marks in total)

1**. The excretion of which of the following drugs is NOT likely to be reduced in an older patient (>65 years of age)?**

- ☐ Atenolol
- ☐ Diazepam
- ☐ Metformin
- ☐ Digoxin

2. With increasing age comes…..

- ☐ A decrease in lean body mass, and body fat in relation to total body weight, as well as, an increase in body water.
- ☐ A decrease in lean body mass, and body water, as well as, an increase in body fat in relation to total body weight.
- ☐ An increase in lean body mass, and body water, as well as, a decrease in body fat in relation to total body weight.
- ☐ An increase in total body fat in relation to total body weight, and body water, as well as, a decrease in lean body mass.

3. In older patients, decreased liver blood flow often leads to....

- ☐ Increased first pass metabolism of water–soluble drugs resulting in lower absorption rates of these drugs.
- ☐ Decreased first pass metabolism of water-soluble drugs resulting in higher absorption of these drugs.
- ☐ Increased first pass metabolism of lipid-soluble drugs resulting in lower rates of absorption for these drugs.
- ☐ Decreased first pass metabolism of lipid-soluble drugs resulting in higher rates of absorption for these drugs.

4. Which of the following drugs is likely to undergo increased distribution in an older patient, leading to a prolonged clinical effect?

- Paracetamol
- Digoxin
- Diazepam
- Atenolol

5. Between the ages of 20 and 70 a person may have up to 50% reduction in renal function. It is this decline in renal function that is the major pharmacokinetic determinant of toxicity in older adult patients. Which measurement is the best indicator of renal function in a 70 year old man with severely reduced muscle mass?

- Cockroft-Gault formula
- MDRD equation
- Serum creatinine
- 24 hour urine output

6. Which of the following best describes the pharmacodynamics associated with anti-hypertensives in older patients?

- Due to a decrease in baroreceptor function, older patients' ability to adjust vascular tone and heart rate in response to volume depletion or vasoactive substances is reduced.
- Due to an increase in baroreceptor function, older patients' ability to adjust vascular tone and heart rate in response to volume depletion or vasoactive substances in increased.
- Due to a decrease in baroreceptor function, older patients may require higher doses of anti-hypertensives to counteract their reduced ability to increase vascular tone.
- Due to an increase in baroreceptor function, older patients may require lower doses of anti-hypertensives.

7. Which of the following is NOT a common adverse drug reaction associated with anxiolytics/hypnotics?

- Falls
- Confusion
- Urinary retention
- Postural hypotension

8. Patients with closed-angle glaucoma should avoid which ONE of the following groups of drugs?

- Non-selective beta-blockers
- Corticosteroids
- Diuretics

- [ ] Tricyclic antidepressants

9. Which group of drugs most predictably increases delirium in older patients?

- [ ] Anti-hypertensives
- [ ] Anti-cholinergic drugs
- [ ] Anti-psychotic drugs
- [ ] Anti-diabetics

10. For how long (maximum) should PPIs be used for at full therapeutic dose post endoscopic diagnosis of duodenal ulcer?

- [ ] 4 weeks
- [ ] 8 weeks
- [ ] 12 weeks
- [ ] No limit

(2 Marks for each correct answer)

Case studies (30 marks in total)

Comment on the appropriateness of the following five prescriptions, and list any changes you would make, or issues you would review, giving your reasons for doing so. These are real life scenarios. There may be multiple points to address in each case

Case 1

80 Year old male

Active problems:
Peptic Ulcer Disease since 2006
Hypertension since 2004
Recurrent gout since 2009
Prostate Carcinoma since 2009

History:
R ankle injury-1992
Diverticular disease 2003
Deep Vein Thrombosis 1999
Regular Medications:
Pantoprazole 40mg od (Since 06)

Bendroflumethiazide/potassium od
Aspirin 75mg od
Paracetamol 500mg 2qds
Glucosamine sachets i od
Prostap 3

Biochemical Data
Total Chol = 2.7 mmol/L
Urea: 8.1 mmol/L
Creatinine: 110micromol/L
Sodium: 147 mmol/L
Potassium: 3.2 mmol/L
eGFR: 59ml/min/1.73m2

PSA 15.8
BP: 130/75 mmHg

1 mark for each of the following points raised……

1. Pantoprazole should be reduced to 20mg once daily
2. Thiazide diuretic inappropriate with gout and metabolic disorder
3. No indication for glucosamine
4. Allopurinol should be considered for gout

Case 2

70 year old male complaining of nausea and sporadic falls

Current Diagnosis:
Hypercholesterolaemia
Ischaemic Heart Disease (IHD)
Insomnia
Gout

History:
Cataracts
MI 2011

Regular medications:
Allopurinol 100mg od
Bendroflumethiazide 2.5mg od
Aspirin 75mg od
Flurazepam 30mg od (past 3 years)

Biochemical Data
eGFR: 30ml/min/1.73m2
Sodium: 136 mmol/L
Potassium: 3.0 mmolL
Urea: 11.2 mmol/L
Creatinine: 140 mmol/L
Urate: 582 micromol/L

1 mark for each of the following points raised:

1. Thiazide diuretic inappropriate with gout
2. Long half-life benzodiazepine inappropriate with history of falls
3. Statin should be considered
4. Beta-blocker should be considered

Case 3

74 year old female complaining of nausea and blackouts

Current Diagnosis:
Paroxysmal Atrial Fibrillation (2007)
Non-obstructive coronary artery disease (coronary angiogram 2007)
Recurrent Gout since 2006 (secondary to thiazide diuretic)
Hypertension
Hypercholesterolaemia
Restless leg syndrome

History:
Non-Hodgkins Lymphoma 2005
Vertigo (single episode) 2011

Regular medications:
Pravastatin 40mg d
Verapamil (slow release) 240mg od
Quinine sulphate 300mg od
Perindopril 5mg/Indapamide 1.5mg od
Digoxin 250mcg od
Diclofenac 75mg bd
Furosemide 20mg od
Betahistine 16mg tds
Paracetamol 1g prn
Warfarin as per INR

Biochemical details:
Fasting Chol: 5.5mmol/L
Urea: 10.4mmol/L
Creatinine: 150 micromol/L
Sodium: 140mmol/L
Potassium: 3.5mmol/L
eGFR: 37ml/min/1.73m2

BP: 105/60 mmHg
HR: 44 BPM
ECG: Sinus rhythm with 1st degree heart block

1 mark for each of the following points raised (+ 1 mark floating for extra points raised):

1. Digoxin dose should be reduced given reduced renal function
2. Digoxin not effective in paroxysmal a-fib.
3. Digoxin and verapamil together is inappropriate
4. Indapamide contraindicated in gout
5. Diclofenac inappropriate given reduced renal function
6. Full dose of betahistine for prolonged period of time
7. Statin dose may be insufficient

Case 4
79 year old male complaining of recent fall and wrist fracture

Diagnoses:
Gout
Insomnia
Hypertension since 1987
Hypercholesterolaemia
OSteoporosis diagnosed in routine screening 2010

History:
Myocardial infarction 2001 no re-vascularisation

Current Medicines:
Allopurinol 300mg od
Olanzapine 2.5mg nocte
Clopidogrel 75mg od
Aspirin 75mg od
Nebivolol 2.5mg od
Doxazosin XL 8mg od
Irbesartan 600mg od
Bendroflumethiazide 2.5mg od
Atorvastatin 10mg od

Biochemical data:
Total Chol: 3.3mmol/L
Urea: 11.8 mmol/L
Creatinine: 161mmol/L
Sodium: 141 mmol/L
Potassium: 4.6mmol/L
eGFR: 38ml/min/1.73m2

Supine BP: 110/70
Standing BP: 85/50

1.5 marks for each of the following points raised (+ 1 mark floating for extra points raised):

1. No indication for dual antiplatelet therapy.
2. Excessive anti-hypertensive therapy-stop alpha blocker
3. No indication for olanzapine
4. Calcium/Vitamin D should be considered given osteoporosis
5. Bisphosphonate should be considered for same

Case 5

77 year old female complaining of recurrent hypos, blackouts, sporadic confusion and chronic constipation

Current diagnosis:
Hypertension since 2004
Non Insulin Dependant Diabetes Mellitus with poor monitoring of glucose
Episode of depression 1989- no relpase

Current Medications:
Aspirin 75mg od
Amlodipine 5mg od
Lisinopril 20mg od
Gliclazide 30mg od
Quetiapine 100mg Bd
Zolpidem 10mg nocte
Glibenclamide 5mg od
Dothiapen 150mg nocte

History:
Previous alcohol abuse-no relapse
Stroke-good recovery-2012

Biochemical Details:
Total Chol: 6.5 mmol/L
Urea: 6.1 mmol/L
Creatinine: 86 mmol/L
Sodium: 138 mmol/L
Potassium 4.5mmol/L
eGFR 60ml/min/1.73m2
LFT normal
No Urinalysis available

BMI: 29.5

1 mark for each of the following points raised:

1. Glibenclamide not the best choice in older patients
2. 2 X Sulfonylureas
3. Constipation possibly casued by quetiapine
4. No indication for quetiapine

5. Metformin may be more appropriate for diabetes in this patient due to obesity
6. Statin should be considered

4 week assessment

1.The excretion of which of the following drugs is likely to be reduced in an older patient (>65 years of age)?

- [ ] Diazepam
- [ ] Nifedipine
- [ ] Digoxin
- [ ] Propranolol

2. With increasing age comes…..

- [ ] A decrease in distribution of lipid-soluble drugs, leading to a hangover effect.
- [ ] An increase in distribution of lipid-soluble drugs, leading to a 'hangover effect'.
- [ ] A decrease in distribution of water-soluble drugs, leading to a 'hangover effect'.
- [ ] An increase in distribution of water-soluble drugs, leading to a 'hangover effect'.

3. Reduction in liver blood flow rate may lead to what, in older patients?

- [ ] Increased first pass metabolism of water–soluble drugs leading to lower absorption rates of these drugs.
- [ ] Decreased first pass metabolism of water-soluble drugs leading to higher absorption of these drugs.
- [ ] Increased first pass metabolism of lipid-soluble drugs leading to lower rates of absorption for these drugs.
- [ ] Decreased first pass metabolism of lipid-soluble drugs leading to higher rates of absorption for these drugs.

4. Which of the following drugs is likely to experience decreased distribution in an older patient?

- [ ] Morphine
- [ ] Digoxin
- [ ] Diazepam
- [ ] Nifedipine

5. Between the ages of 20 and 70 a person may have up to 50% reduction in renal function. In practice it is this decline in renal function that is the major pharmacokinetic determinant of toxicity in older adult patients. Which measure should be used to estimate kidney function in a 70 year old man with severely reduced muscle mass?

- [ ] Creatinine clearance
- [ ] eGFR

6. Which of the following best describes the pharmacodynamics associated with anti-psychotics in older patients?

- [ ] Due to an increase in dopamine (1 and 2) receptors, extrapyramidal side-effects of anti-psychotics are increased.
- [ ] Due to a decrease in dopamine (1 and 2) receptors, extrapyramidal side effects- of anti-psychotics are increased.
- [ ] Due to an increase in dopamine (1 and 2) receptors, extrapyramidal side effects of anti-psychotics are decreased.
- [ ] Due to a decrease in dopamine (1 and 2) receptors, extrapyramidal side effects of anti-psychotics are decreased.

7. Memory loss, constipation, urinary retention and exacerbation of glaucoma are most commonly associated with which family of drugs?

- [ ] NSAIDs
- [ ] Hypnotics
- [ ] Anit-muscarinincs
- [ ] Opioid analgesics

8. Patients with pre-existing dementia should avoid which ONE of the following groups of drugs?

- [ ] Calcium-channel blockers
- [ ] Anti-psychotics
- [ ] Diuretics
- [ ] Tricyclic antidepressants

9. Which group of drugs should be avoided in patients with a history of clinically significant hyponatremia?

- [ ] Non- selective beta-blockers
- [ ] Serotonin selective re-uptake inhibitors
- [ ] Opioid analgesics
- [ ] Anti-diabetics

10. What is the max dose of Aspirin for a patient aged 65 or older?

- [ ] 75mg
- [ ] 150mg
- [ ] 225mg
- [ ] 300mg

(2 marks for each correct answer)

Case studies (30 marks in total)

Case 1

70 year old male complaining of nausea and blackouts

Current Diagnosis:
Paroxysmal Atrial Fibrillation (2007)
Non-obstructive coronary artery disease (coronary angiogram 2007)
Recurrent Gout since 2006 (secondary to thiazide diuretic)
Hypertension
Hypercholesterolaemia
Restless leg syndrome
Worsening asthma

History:
Non-Hodgkins Lymphoma 2005
Duodenal ulcer-resolved

Regular medications:
Pravastatin 40mg d
Verapamil (slow release) 240mg od
Quinine sulphate 300mg od

Perindopril 5mg/Indapamide 1.5mg od
Digoxin 250mcg od
Inegy 10/20 od
Omeprazole 40mg BD
Diclofenac 75mg bd
Furosemide 20mg od
Paracetamol 1g prn
Warfarin as per INR

Biochemical details:
Fasting Chol: 3.8mmol/L
Urea: 10.4mmol/L
Creatinine: 150 micromol/L
Sodium: 140mmol/L
Potassium: 3.5mmol/L
eGFR: 37ml/min/1.73m2

BP: 105/60 mmHg
HR: 44 BPM
ECG: Sinus rhythm with 1st degree heart block

1 mark for each of the following points raised (+ 1 mark floating for extra points raised…..

1. Digoxin not effective in paroxysmal a-fib
2. Digoxin and verapamil together is inappropriate
3. PPI at max strength for resolved duodenal ulcer
4. Diclofenac with reduced renal function
5. 2 x statins
6. Requires asthma therapy
7. Digoxin dose too high given reduced renal function

Case 2

71 Year old male complaining of constipation

Active problems:
Peptic Ulcer Disease since 2006
Hypertension since 2004
Prostate Carcinoma since 2009
Moderate depression diagnosed 6 months ago
Diverticular disease with sporadic constipation

History:
R ankle injury-1992
Deep Vein Thrombosis 1999

Regular Medications:
Pantoprazole 40mg od (Since 06)
Bendroflumethiazide 2.5mg od
Aspirin 75mg od
Paracetamol 500mg 2qds
Amitriptyline 25mg

Prostap 3 (leuprorelin)

Biochemical Data
Total Chol = 2.7 mmol/L
Urea: 8.1 mmol/L
Creatinine: 110micromol/L
Sodium: 147 mmol/L
Potassium: 3.2 mmol/L
eGFR: 59ml/min/1.73m2

PSA 15.8
BP: 130/75 mmHg

1 mark for each of the following points raised (+ 1 mark floating for extra points raised)

1. PPI dose should be reduced to 20mg daily
2. Thiazide diuretic not appropriate with metabolic derangement
3. Amitriptyline inappropriate with constipation
4. Fibre supplement should be considered

Case 3

73 year old female complaining of recurrent hypos, blackouts, sporadic confusion and chronic constipation

Current diagnosis:
Hypertension since 2004
Non Insulin Dependant Diabetes Mellitus with poor monitoring of glucose
Recent episode of depression

History:
Previous alcohol abuse-no relapse
Stroke-good recovery-2012

Current Medications:
Aspirin 75mg od
Atenolol 25mg od
Lisinopril 20mg od
Citalopram 10mg od
Gliclazide 30mg od
Quetiapine 100mg Bd
Zolpidem 10mg nocte
Dothiapen 150mg nocte

Biochemical Details:
Total Chol: 6.5 mmol/L
Urea: 6.1 mmol/L
Creatinine: 86 mmol/L
Sodium: 110 mmol/L
Potassium 4.5mmol/L
eGFR 60ml/min/1.73m2
LFT normal
No Urinalysis available

BMI: 29.5

1 mark for each of the following points raised:

1. Beta-blocker inappropriate with diabetes.
2. Citalopram inappropriate with decreased renal function
3. Constipation possibly caused by quetiapine
4. No indication for quetiapine
5. Metformin may be better anti-diabetic as patient is obese
6. Statin should be considered

Case 4

77 year old female complaining of nausea and sporadic falls

Current Diagnosis:
Hypercholesterolaemia
Ischaemic Heart Disease (IHD)
Insomnia
Gout

History:
Cataracts
MI 2011

Regular medications:
Allopurinol 100mg od
Bendroflumethiazide 2.5mg od
Aspirin 75mg od
Flurazepam 30mg od (past 3 years)

Biochemical Data
eGFR: 30ml/min/1.73m2
Sodium: 136 mmol/L
Potassium: 3.0 mmolL
Urea: 11.2 mmol/L
Creatinine: 140 mmol/L
Urate: 582 micromol/L

Fasting Chol: 6.8mmol/L

1 mark for each of the following points raised:

1. Thiazide diuretic inappropriate with gout
2. Long half-life benzodiazepine inappropriate with history of falls
3. Statin should be considered
4. Beta-blocker should be considered

Case 5

79 year old male complaining of recent fall and wrist fracture

Diagnoses:
Gout
Insomnia
Hypertension since 1987
Hypercholesterolaemia
Osteoporosis diagnosed in routine screening 2010
Recent urinary incontinence-daily occurrence
Mild allergies

History:
Myocardial infarction 2001 no re-vascularisation

Current Medicines:
Allopurinol 300mg od
Olanzapine 2.5mg nocte
Aspirin 75mg od
Nebivolol 2.5mg od
Doxazosin XL 8mg od
Irbesartan 600mg od
Bendroflumethiazide 2.5mg od
Atorvastatin 10mg od
Chlorphenamine 4mg tds

Biochemical data:
Total Chol: 3.3mmol/L
Urea: 11.8 mmol/L
Creatinine: 161mmol/L
Sodium: 141 mmol/L
Potassium: 4.6mmol/L
eGFR: 38ml/min/1.73m2

1.5 marks for each of the following points raised (+ 1.5 marks floating for extra points raised):

1. Alpha blocker inappropriate with incontinence

2. Chlorphenermine long term is inappropriate

3. No indication for olanzapine

4. Calcium/Vitamin D should be considered for osteoporosis

5. Bisphosphonates should be considered for same

12 Week assessment

1. The excretion of which drugs is likely to be reduced in an older patient (>65 years of age)?

- [ ] Lipid-soluble
- [ ] Water-soluble

2. With increasing age, drugs bound to muscle may

- [ ] Experience increased distribution leading to a hang-over effect.
- [ ] Experience decreased distribution leading to a hang-over effect.
- [ ] Experience increased distribution thereby requiring an increase in dose
- [ ] Experience decreased distribution thereby requiring a decrease in dose.

3. The bioavailability of which one of these drugs is unlikely to be affected by age?

- [ ] Nifedipine
- [ ] Atenolol
- [ ] Propranolol
- [ ] Morphine

4. Why is this so?

- [ ] It is a lipid-soluble drug therefore experiences decreased distribution in an older patient
- [ ] It is a water soluble drug therefore not affected by reduced liver blood flow rate
- [ ] It is a lipid soluble drug therefore not affected by liver blood flow rate
- [ ] It is a water soluble drug therefore experiences increased distribution in an older adult.

5. Between the ages of 20 and 70 a person may have up to 50% reduction in renal function. In practice it is this decline in renal function that is the major pharmacokinetic determinant of toxicity in older adult patients.Which measure should be used to estimate kidney function in a 70 year old man with severely reduced muscle mass?

- [ ] Creatinine clearance
- [ ] eGFR

6. Which of the following best describes the pharmacodynamics associated with opioids in older patients?

- [ ] Due to a decrease in opioid receptors, likelihood of behavioural changes is increased in older patients.
- [ ] Due to an increase in opioid receptors, likelihood of behavioural changes is increased in older patients.

7. Falls, confusion and postural hypotension are most commonly associated with which family of drugs?

- [ ] NSAIDs
- [ ] Hypnotics/anxiolytics
- [ ] Anit-muscarinincs
- [ ] Opioid analgesics

8. Patients with pre-existing dementia should avoid which ONE of the following groups of drugs?

- [ ] Calcium-channel blockers
- [ ] Anti-histamines
- [ ] Anti-psychotics
- [ ] NSAIDs

9. With regards to proton pump inhibitors, which of the following is true?

- [ ] They should not be used for more than eight weeks in older patients.
- [ ] They should not be used at all in older patients.

☐ The max therapeutic dose can be used for up to eight weeks, after which, the dose should be reduce to a maintenance dose.

☐ The max therapeutic dose can be used for up to twelve weeks, after which, the dose should be reduce to a maintenance dose.

10. True or false, ACE inhibitors are considered appropriate for older patients with chronic heart failure?

☐ True

☐ False

(2 marks for each correct answer)

Case studies (30 marks total)

Case 1

70 year old male complaining of nausea and sporadic falls

Current Diagnosis:
Hypercholesterolaemia
Ischaemic Heart Disease (IHD)
Insomnia
Gout

History:
Cataracts
MI 2011

Regular medications:
Allopurinol 100mg od
Bendroflumethiazide 2.5mg od
Aspirin 75mg od
Flurazepam 30mg od (past 3 years)

Biochemical Data
eGFR: 30ml/min/1.73m2
Sodium: 136 mmol/L

Potassium: 3.0 mmolL
Urea: 11.2 mmol/L
Creatinine: 140 mmol/L
Urate: 582 micromol/L

Fasting Chol: 6.8mmol/L

1 mark for each of the following points raised…….

1. Thiazide diuretic inappropriate with gout
2. Long half-life benzodiazepine inappropriate with history of falls
3. Patient not taking any statin
4. Patient not taking any benzodiazepine

Case 2

72 year old male complaining of recent fall and wrist fracture

Diagnoses:
Gout
Hypertension since 1987
Hypercholesterolaemia
Osteoporosis diagnosed in routine screening 2010
Glaucoma
Depression

History:
Myocardial infarction 2001 no re-vascularisation

Current Medicines:
Allopurinol 300mg od
Aspirin 300mg od
Nebivolol 2.5mg od
Doxazosin XL 8mg od
Irbesartan 600mg od
Bendroflumethiazide 2.5mg od
Atorvastatin 10mg od
Amitriptyline 25mg nocte
Xalatan eye drops nocte

Biochemical data:
Total Chol: 3.3mmol/L
Urea: 11.8 mmol/L
Creatinine: 161mmol/L
Sodium: 141 mmol/L
Potassium: 4.6mmol/L
eGFR: 38ml/min/1.73m2

Supine BP: 110/70
Standing BP: 85/50

1.5 marks for each of the following points raised (+1.5 marks for extra points raised):

1. No benefit to aspirin dose > 150mg
2. TCA inappropriate with glaucoma
3. Excessive antihypertensive therapy
4. Calcium/Vitamin D should be considered for osteoporosis
5. Bisphosphonate should be considered for same

Case 3

74 year old female complaining of recurrent hypos, blackouts, sporadic confusion, worsening COPD.

Current diagnosis:
Hypertension since 2004
Non Insulin Dependant Diabetes Mellitus with poor monitoring of glucose
COPD
Glaucoma

Current Medications:
Aspirin 300mg od
Amlodipine 5mg od
Lisinopril 20mg od
Gliclazide 30mg od
Zolpidem 10mg nocte
Propranolol 10mg od
Dothiapen 150mg nocte
Ventolin inhaler 2puffs qds prn
Atrovent nebules od (new)
Seretide 250 inhaler bd
Xalatan eye drops one drop nocte

History:
Previous alcohol abuse-no relapse
Stroke-good recovery-2012

Biochemical Details:
Total Chol: 6.5 mmol/L
Urea: 6.1 mmol/L
Creatinine: 86 mmol/L
Sodium: 138 mmol/L
Potassium 4.5mmol/L
eGFR 60ml/min/1.73m2
LFT normal
No Urinalysis available

BMI: 29.5

1 mark for each of the following points raised:

1. Beta-blocker inappropriate in diabetes
2. Beta-blocker inappropriate in COPD
3. Nebulised Atrovent inappropriate with glaucoma
4. No benefit to aspirin dose greater than 150mg
5. Metformin may be a better anti-diabetic as patient is obese
6. Statin should be considered

Case 4

80 Year old male complaining of constipation

Active problems:
Peptic Ulcer Disease since 2006
Hypertension since 2004
Recurrent gout since 2009
Prostate Carcinoma since 2009
Depression for last 6 months

History:
R ankle injury-1992
Diverticular disease 2003
Deep Vein Thrombosis 1999

Regular Medications:
Allopurinol 100mg od
Pantoprazole 40mg od (Since 06)
Bendroflumethiazide/potassium od
Aspirin 75mg od
Paracetamol 500mg 2qds
Verapamil 120mg od
Prostap 3

Biochemical Data
Total Chol = 2.7 mmol/L
Urea: 8.1 mmol/L
Creatinine: 110micromol/L
Sodium: 147 mmol/L
Potassium: 3.2 mmol/L
eGFR: 59ml/min/1.73m2

PSA 15.8
BP: 130/75 mmHg

1 mark for each of the following points rasied:

1. PPI needs to be reduced to 20mg daily
2. Thiazide diuretic inappropriate in presence of gout and metabolic disorder.
3. Verapamil may be causing constipation
4. Antidepressant may be required for depression

Case 5

76 year old female complaining of nausea and blackouts

Current Diagnosis:
Paroxysmal Atrial Fibrillation (2007)
Non-obstructive coronary artery disease (coronary angiogram 2007)
Recurrent Gout since 2006 (secondary to thiazide diuretic)
Hypertension
Hypercholesterolaemia
Restless leg syndrome

History:
Non-Hodgkins Lymphoma 2005
Vertigo (single episode) 2011

Regular medications:
Pravastatin 40mg od
Verapamil (slow release) 240mg od
Quinine sulphate 300mg od
Perindopril 5mg/Indapamide 1.5mg od
Digoxin 250mcg od
Diclofenac 75mg bd
Furosemide 20mg od
Betahistine 16mg tds
Paracetamol 1g prn
Warfarin as per INR

Biochemical details:
Fasting Chol: 6.0 mmol/L
Urea: 10.4mmol/L
Creatinine: 150 micromol/L
Sodium: 140mmol/L
Potassium: 3.5mmol/L
eGFR: 37ml/min/1.73m2

BP: 105/60 mmHg
HR: 44 BPM
ECG: Sinus rhythm with 1st degree heart block

1.5 marks for each of the following points raised (+1.5 marks floating for extra points raised):

1. Digoxin dose should be reduced given reduced renal function
2. Digoxin not effective in paroxysmal a-fib.
3. Digoxin and verapamil together is inappropriate
4. Indapamide contraindicated in gout
5. Diclofenac inappropriate given reduced renal function
6. Full dose of betahistine for prolonged period of time
7. Statin dose may be insufficient

11.12 Appendix XII: CONSORT checklist for RCTs



CONSORT 2010 checklist of information to include when reporting a randomised trial*

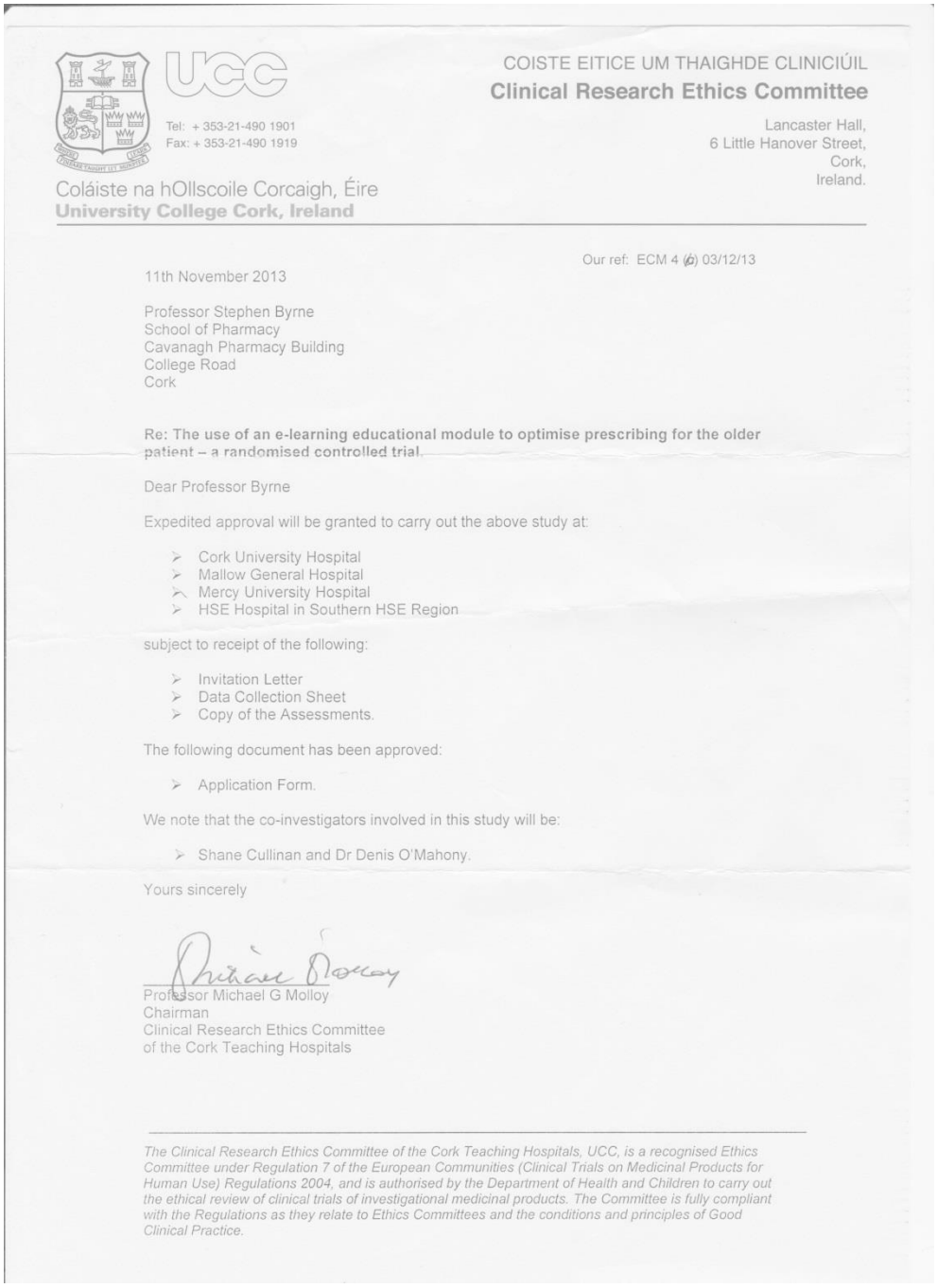
Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	

Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	

Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	
	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	

Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

11.13 Appendix XIII: Ethics approval for Chapter 4 Research



UCC

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COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Our ref: ECM 4 (p) 03/12/13

11th November 2013

Professor Stephen Byrne
School of Pharmacy
Cavanagh Pharmacy Building
College Road
Cork

Re: The use of an e-learning educational module to optimise prescribing for the older patient – a randomised controlled trial.

Dear Professor Byrne

Expedited approval will be granted to carry out the above study at:

- Cork University Hospital
- Mallow General Hospital
- Mercy University Hospital
- HSE Hospital in Southern HSE Region

subject to receipt of the following:

- Invitation Letter
- Data Collection Sheet
- Copy of the Assessments.

The following document has been approved:

- Application Form.

We note that the co-investigators involved in this study will be:

- Shane Cullinan and Dr Denis O'Mahony.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (w) 04/02/14

20th January 2014

Professor Stephen Byrne
School of Pharmacy
Cavanagh Pharmacy Building
College Road
Cork

Re: The use of an e-learning educational module to optimise prescribing for the older patient – a randomised controlled trial.

Dear Professor Byrne

The Chairman approved the following:

- Invitation Letter
- Data Collection Sheet
- Copy of the Assessments.

Full approval is now granted to carry out the above study.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant

Ollscoil na hÉireann, Corcaigh - National University of Ireland, Cork.

11.14 Appendix XIV: STOPP/START criteria versions 1 & 2

STOPP

Screening Tool of Older People's potentially inappropriate Prescriptions

The following prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

A. Cardiovascular System

1. Digoxin at a long-term dose > 125 micrograms/day with impaired renal function* *(increased risk of toxicity).*
2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure *(no evidence of efficacy, compression hosiery usually more appropriate).*
3. Loop diuretic as first-line monotherapy for hypertension *(safer, more effective alternatives available).*
4. Thiazide diuretic with a history of gout *(may exacerbate gout).*
5. Beta-blocker with Chronic Obstructive Pulmonary Disease (COPD) *(risk of increased bronchospasm).*
6. Beta-blocker in combination with verapamil *(risk of symptomatic heart block).*
7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure *(may worsen heart failure).*
8. Calcium-channel blockers with chronic constipation *(may exacerbate constipation).*
9. Use of aspirin and warfarin in combination without histamine H_2 receptor antagonist (except cimetidine because of interaction with warfarin) or Proton Pump Inhibitor (PPI) *(high risk of gastrointestinal bleeding).*
10. Dipyridamole as monotherapy for cardiovascular secondary prevention *(no evidence for efficacy).*
11. Aspirin with a past history of peptic ulcer disease without histamine H_2 receptor antagonist or PPI *(risk of bleeding).*
12. Aspirin at dose > 150 mg day *(increased bleeding risk, no evidence for increased efficacy).*
13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event *(not indicated).*
14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease *(not indicated).*
15. Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration *(no proven added benefit).*
16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration *(no proven benefit).*

17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder *(high risk of bleeding).*

* estimated GFR less than 50 ml/min

B. Central Nervous System and Psychotropic Drugs

1. Tricyclic antidepressants (TCAs) with dementia *(risk of worsening cognitive impairment).*
2. TCAs with glaucoma *(likely to exacerbate glaucoma).*
3. TCAs with cardiac conductive abnormalities *(pro-arrhythmic effects).*
4. TCAs with constipation *(likely to worsen constipation).*
5. TCAs with an opiate or calcium channel blocker *(risk of severe constipation).*
6. TCAs with prostatism or prior history of urinary retention *(risk of urinary retention).*
7. Long-term (i.e. > 1 month), long-acting benzodiazepines (e.g. chlordiazepoxide, flurazepam, nitrazepam) and those with long-acting metabolites (e.g. diazepam) *(risk of prolonged sedation, confusion, impaired balance, falls).*
8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics *(risk of confusion, hypotension, extra-pyramidal side-effects, falls).*
9. Long-term neuroleptics (> 1 month) in those with parkinsonism *(likely to worsen extra-pyramidal symptoms (EPSE)).*
10. Phenothiazines in patients with epilepsy *(may lower seizure threshold).*
11. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications *(risk of anticholinergic toxicity).*
12. Selective serotonin re-uptake inhibitors (SSRIs) with a history of clinically significant hyponatraemia *(non-iatrogenic hyponatraemia <130mmol/l within the previous 2 months).*
13. Prolonged use (> 1 week) of first generation antihistamines i.e. diphenhydramine, chlorphenamine, cyclizine, promethazine *(risk of sedation and anti-cholinergic side-effects).*

C. Gastrointestinal System

1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause *(risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognised gastroenteritis).*
2. Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity *(risk of exacerbation or protraction of infection).*

3. Prochlorperazine (Stemetil®) or metoclopramide with Parkinsonism *(risk of exacerbating Parkinsonism).*

4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks *(dose reduction or earlier discontinuation indicated).*

5. Anticholinergic antispasmodic drugs with chronic constipation *(risk of exacerbation of constipation).*

D. Respiratory System

1. Theophylline as monotherapy for COPD *(safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).*

2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD *(unnecessary exposure to long-term side-effects of systemic steroids).*

3. Nebulised ipratropium with glaucoma *(may exacerbate glaucoma).*

E. Musculoskeletal System

1. Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H_2 receptor antagonist, PPI or misoprostol *(risk of peptic ulcer relapse).*

2. NSAID with moderate-severe hypertension (moderate: 160/100 mmHg – 179/109 mmHg; severe: ≥180/110 mmHg) *(risk of exacerbation of hypertension).*

3. NSAID with heart failure *(risk of exacerbation of heart failure).*

4. Long-term use of NSAID (>3 months) for relief of mild joint pain in osteoarthritis *(simple analgesics preferable and usually as effective for pain relief).*

5. Warfarin and NSAID together *(risk of gastrointestinal bleeding).*

6. NSAID with chronic renal failure* *(risk of deterioration in renal function).*

* estimated GFR 20-50 ml/min

7. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis or osteoarthritis *(risk of major systemic corticosteroid side-effects).*

8. Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol *(allopurinol first choice prophylactic drug in gout).*

F. Urogenital System

1. Bladder antimuscarinic drugs with dementia *(risk of increased confusion, agitation).*

2. Antimuscarinic drugs with chronic glaucoma *(risk of acute exacerbation of glaucoma).*

3. Antimuscarinic drugs with chronic constipation *(risk of exacerbation of constipation).*

4. Antimuscarinic drugs with chronic prostatism *(risk of urinary retention).*

5. Alpha-blockers in males with frequent incontinence i.e. one or more episodes of incontinence daily *(risk of urinary frequency and worsening of incontinence).*

6. Alpha-blockers with long-term urinary catheter *in situ* i.e. more than 2 months *(drug not indicated).*

G. Endocrine System

1. Glibenclamide or chlorpropamide with Type 2 diabetes mellitus *(risk of prolonged hypoglycaemia).*

2. Beta-blockers in those with diabetes mellitus and frequent hypoglycaemic episodes i.e. ≥ 1 episode per month *(risk of masking hypoglycaemic symptoms).*

3. Oestrogens with a history of breast cancer or venous thromboembolism *(increased risk of recurrence).*

4. Oestrogens without progestogen in patients with intact uterus *(risk of endometrial cancer).*

H. Drugs that adversely affect those prone to falls (≥ 1 fall in past three months)

1. Benzodiazepines *(sedative, may cause reduced sensorium, impair balance).*

2. Neuroleptic drugs *(may cause gait dyspraxia, Parkinsonism).*

3. First generation antihistamines *(sedative, may impair sensorium).*

4. Vasodilator drugs known to cause hypotension in those with persistent postural hypotension i.e. recurrent > 20 mmHg drop in systolic blood pressure *(risk of syncope, falls).*

5. Long-term opiates in those with recurrent falls *(risk of drowsiness, postural hypotension, vertigo).*

I. Analgesic Drugs

1. Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain *(WHO analgesic ladder not observed).*

2. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives *(risk of severe constipation).*

3. Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome *(risk of exacerbation of cognitive impairment).*

J. Duplicate Drug Classes

Any duplicate drug class prescription e.g. two concurrent opiates, NSAIDs, SSRIs, loop diuretics, ACE inhibitors *(optimisation of monotherapy within a single drug class should be observed prior to considering a new class of drug).*

START

Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatments

These medications should be considered for people ≥ 65 years of age with the following conditions, where no contraindication to prescription exists.

A. Cardiovascular System

1. Warfarin in the presence of chronic atrial fibrillation.
2. Aspirin in the presence of chronic atrial fibrillation, where warfarin is contraindicated (but aspirin is not).
3. Aspirin or clopidogrel with a documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm.
4. Antihypertensive therapy where systolic blood pressure is consistently >160 mmHg.
5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is > 5 years.
6. Angiotensin Converting Enzyme (ACE) inhibitor with chronic heart failure.
7. ACE inhibitor following acute myocardial infarction.
8. Beta-blocker with chronic stable angina.

B. Respiratory System

1. Regular inhaled $beta_2$ agonist or anticholinergic agent for mild to moderate asthma or COPD.
2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where predicted FEV1 <50%.
3. Home continuous oxygen with documented chronic type 1 respiratory failure (pO_2 < 8.0 kPa, pCO_2 <6.5 kPa) or type 2 respiratory failure (pO_2 < 8.0 kPa, pCO_2 > 6.5 kPa).

C. Central Nervous System

1. L-DOPA in idiopathic Parkinson's disease with definite functional impairment and resultant disability.
2. Antidepressant drug in the presence of moderate-severe depressive symptoms lasting at least three months.

D. Gastrointestinal System

1. Proton Pump Inhibitor with severe gastro-oesophageal acid reflux disease or peptic stricture requiring dilatation.
2. Fibre supplement for chronic, symptomatic diverticular disease with constipation.

E. Musculoskeletal System

1. Disease-modifying anti-rheumatic drug (DMARD) with active moderate-severe rheumatoid disease lasting > 12 weeks.
2. Bisphosphonates in patients taking maintenance corticosteroid therapy.
3. Calcium and Vitamin D supplement in patients with known osteoporosis (previous fragility fracture, acquired dorsal kyphosis).

F. Endocrine System

1. Metformin with Type 2 diabetes +/- metabolic syndrome (in the absence of renal impairment*).
2. ACE inhibitor or Angiotensin Receptor Blocker in diabetes with nephropathy i.e. overt urinalysis proteinuria or microalbuminuria (>30 mg/24 hours) +/- serum biochemical renal impairment*.
3. Antiplatelet therapy in diabetes mellitus with co-existing major cardiovascular risk factors (hypertension, hypercholesterolaemia, smoking history).
4. Statin therapy in diabetes mellitus if co-existing major cardiovascular risk factors present.

* estimated GFR less than 50 ml/min

STOPP/START Version 2

Appendix 3: Screening Tool of Older Persons' Prescriptions (STOPP) version 2.

The following prescriptions are potentially inappropriate to use in patients aged 65 years and older.

Section A: Indication of medication

1. Any drug prescribed without an evidence-based clinical indication.

2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.

3. Any duplicate drug class prescription e.g. two concurrent NSAIDs, SSRIs, loop diuretics, ACE inhibitors, anticoagulants (optimisation of monotherapy within a single drug class should be observed prior to considering a new agent).

Section B: Cardiovascular System

1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)

2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).

3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).

4. Beta blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole).

5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)

6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).

7. Loop diuretic for dependent ankle oedema without clinical, biochemical evidence or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and /or compression hosiery usually more appropriate).

8. Thiazide diuretic with current significant hypokalaemia (i.e. serum $K^+ < 3.0$ mmol/l), hyponatraemia (i.e. serum $Na^+ < 130$ mmol/l) hypercalcaemia (i.e. corrected serum calcium > 2.65 mmol/l) or with a history of gout (hypokalaemia, hyponatraemia, hypercalcaemia and gout can be precipitated by thiazide diuretic)

9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).

10. Centrally-acting antihypertensives (e.g. methyldopa, clonidine, moxonidine, rilmenidine, guanfacine), unless clear intolerance of, or lack of efficacy with, other classes of antihypertensives (centrally-active antihypertensives are generally less well tolerated by older people than younger people)

11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.

12. Aldosterone antagonists (e.g. spironolactone, eplerenone) with concurrent potassium-conserving drugs (e.g. ACEI's, ARB's, amiloride, triamterene) without monitoring of serum potassium (risk of dangerous hyperkalaemia i.e. > 6.0 mmol/l – serum K should be monitored regularly, i.e. at least every 6 months).

13. Phosphodiesterase type-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent nitrate therapy for angina (risk of cardiovascular collapse)

Section C: Antiplatelet/Anticoagulant Drugs

1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).

2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).

3. Aspirin, clopidogrel, dipyridamole, vitamin K antagonists, direct thrombin inhibitors or factor Xa inhibitors with concurrent significant bleeding risk, i.e. uncontrolled severe hypertension, bleeding diathesis, recent non-trivial spontaneous bleeding) (high risk of bleeding).

4. Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy)

5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation (no added benefit from aspirin)

6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (No added benefit from dual therapy).

7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).

8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (e.g. thrombophilia) for > 6 months, (no proven added benefit).

9. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (e.g. thrombophilia) for > 12 months (no proven added benefit).

10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of major gastrointestinal bleeding).

11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease)

Section D: Central Nervous System and Psychotropic Drugs

1. TriCyclic Antidepressants (TCAs) with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).

2. Initiation of TriCyclic Antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).

3. Neuroleptics with moderate-marked antimuscarinic/anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenzine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).

4. Selective serotonin re-uptake inhibitors (SSRI's) with current or recent significant hyponatraemia i.e. serum Na+ < 130 mmol/l (risk of exacerbating or precipitating hyponatraemia).

5. Benzodiazepines for ≥ 4 weeks (no indication for longer treatment; risk of prolonged sedation, confusion, impaired balance, falls, road traffic accidents; all benzodiazepines should be withdrawn gradually if taken for more than 4 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).

6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms)

7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity),

8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).

9. Neuroleptic antipsychotic in patients with behavioural and psychological symptoms of dementia (BPSD) unless symptoms are severe and other non-pharmacological treatments have failed (increased risk of stroke).

10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).

11. Acetylcholinesterase inhibitors with a known history of persistent bradycardia (< 60 beats/min.), heart block or recurrent unexplained syncope or concurrent treatment with drugs that reduce heart rate such as beta-blockers, digoxin, diltiazem, verapamil (risk of cardiac conduction failure, syncope and injury).

12. Phenothiazines as first-line treatment, since safer and more efficacious alternatives exist (phenothiazines are sedative, have significant anti-muscarinic toxicity in older people, with the exception of prochlorperazine for nausea/vomiting/vertigo, chlorpromazine for relief of persistent hiccoughs and levomepromazine as an anti-emetic in palliative care).

13. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy)

14. First-generation antihistamines (safer, less toxic antihistamines now widely available).

Section E: Renal System. The following drugs are potentially inappropriate in older people with acute or chronic kidney disease with renal function below particular levels of eGFR (refer to summary of product characteristics datasheets and local formulary guidelines)

1. Digoxin at a long-term dose greater than 125µg/day if eGFR < 30 ml/min/1.73m2 (risk of digoxin toxicity if plasma levels not measured).

2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding)

3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding)

4. NSAID's if eGFR < 50 ml/min/1.73m2 (risk of deterioration in renal function).

5. Colchicine if eGFR < 10 ml/min/1.73m2 (risk of colchicine toxicity)

6. Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis).

Section F: Gastrointestinal System

1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).

2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).

3. Drugs likely to cause constipation (e.g. antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation).

4. Oral elemental iron doses greater than 200 mg daily (e.g. ferrous fumarate> 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate> 1800 mg/day; no evidence of enhanced iron absorption above these doses).

Section G: Respiratory System

1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).

2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD (unnecessary exposure to long-term side-effects of systemic corticosteroids and effective inhaled therapies are available).

3. Anti-muscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention).

4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).

5. Benzodiazepines with acute or chronic respiratory failure i.e. $pO2 < 8.0$ kPa ± $pCO2 > 6.5$ kPa (risk of exacerbation of respiratory failure).

Section H: Musculoskeletal System

1. Non-steroidal anti-inflammatory drug (NSAID) other than COX-2 selective agents with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent PPI or H2 antagonist (risk of peptic ulcer relapse).

2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).

3. Long-term use of NSAID (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief)

4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis (risk of systemic corticosteroid side-effects).

5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).

6. Long-term NSAID or colchicine (>3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor (e.g. allopurinol, febuxostat) (xanthine-oxidase inhibitors are first choice prophylactic drugs in gout).

7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke)

8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease)

9. Oral bisphosphonates in patients with a current or recent history of upper gastrointestinal disease i.e. dysphagia, oesophagitis, gastritis, duodenitis, or peptic ulcer disease, or upper gastrointestinal bleeding (risk of relapse/exacerbation of oesophagitis, oesophageal ulcer, oesophageal stricture)

Section I: Urogenital System

1. Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention).

2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)

Section J. Endocrine System

1. Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).

2. Thiazolidenediones (e.g. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure)

3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).

4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).

5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).

6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of the hypogonadism indication).

Section K: Drugs that predictably increase the risk of falls in older people

1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).

2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).

3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers,) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).

4. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).

Section L: Analgesic Drugs

1. Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine, pentazocine) as first line therapy for mild pain (WHO analgesic ladder not observed).

2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation).

3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain)

Section N: Antimuscarinic/Anticholinergic Drug Burden

Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties (e.g. bladder antispasmodics, intestinal antispasmodics, tricyclic antidepressants, first generation antihistamines) (risk of increased antimuscarinic/anticholinergic toxicity)

Appendix: 4: Screening Tool to Alert to Right Treatment (START), version 2.

Unless an elderly patient's clinical status is end-of-life and therefore requiring a more palliative focus of pharmacotherapy, the following drug therapies should be considered where omitted for no valid clinical reason(s). It is assumed that the prescriber observes all the specific contraindications to these drug therapies prior to recommending them to older patients.

Section A: Cardiovascular System

1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.

2. Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated.

3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.

4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently >90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic.

5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years.

6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.

7. Beta-blocker with ischaemic heart disease.

8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol or carvedilol) with stable systolic heart failure.

Section B: Respiratory System

1. Regular inhaled 2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild to moderate asthma or COPD.

2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids.

3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%)

Section C: Central Nervous System& Eyes

1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability.

2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.

3. Acetylcholinesterase inhibitor (e.g. donepezil, rivastigmine, galantamine) for mild-moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).

4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.

5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.

6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.

Section D: Gastrointestinal System

1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.

2. Fibre supplements (e.g. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation.

Section E: Musculoskeletal System

1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.

2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.

3. Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than -2.5 in multiple sites).

4. Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (Bone Mineral Density T-scores -> 2.5 in multiple sites) and/or previous history of fragility fracture(s).

5. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia (Bone Mineral Density T-score is > -1.0 but < -2.5 in multiple sites).

6. Xanthine-oxidase inhibitors (e.g. allopurinol, febuxostat) with a history of recurrent episodes of gout.

7. Folic acid supplement in patients taking methotexate.

Section F: Endocrine System

1. ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment.

Section G: Urogenital System

1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary.

2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary.

3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.

Section H: Analgesics

1. High-potency opioids in moderate-severe pain, where paracetamol, NSAIDs or low-potency opioids are not appropriate to the pain severity or have been ineffective.

2. Laxatives in patients receiving opioids regularly.

Section I: Vaccines

1. Seasonal trivalent influenza vaccine annually

2. Pneumococcal vaccine at least once after age 65 according to national guidelines

11.15 Appendix XV: Ethics approval for Chapter 5 research

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Our ref: ECM 3 (IIIII) 04/03/14

3rd March 2014

Dr Denis O'Mahony
Senior Lecturer
Department of Geriatric Medicine
Cork University Hospital
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Cork

Re: SENATOR Study.

Dear Dr O'Mahony

The Chairman approved the following:

- Revised Study Protocol Version 6
- Information Leaflet/Consent Form.

Full approval is granted to implement this amendment.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

CORK UNIVERSITY HOSPITAL
13 MAR 2014

11.16 Appendix XVI: Ethics approval for Chapter 6 research

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13 MAR 2014

11.17 Appendix XVII: Ethics approval for Chapter 7 research

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