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The role of the pharmacist in optimising prescribing in community-dwelling older adults.

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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

August 2017

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List of Abbreviations

ACB	Anticholinergic cognitive burden
AD	Academic detailing
ADE	Adverse drug event
ADR	Adverse drug reaction
BMI	Body mass index
CDSS	Computerised decision support systems
CME	Continuing medical education
COREQ	Consolidated criteria for reporting qualitative research
DBI	Drug burden index
EPOC	Effective Practice and Organisation of Care
GMS	General Medical Services
GP	General Practitioner
GRAMMS	Good Reporting of a Mixed Methods Study
HCP	Healthcare professional
HSE	Health Service Executive
ICGP	Irish College of General Practitioners
ICS	International Continence Society
INR	International normalised ratio
ITS	Interrupted time series
LUTS	Lower urinary tract symptoms
MAI	Medication Appropriateness Index
NaRCAD	National Resource Center for Academic Detailing
PDRM	Preventable drug-related morbidity

PFMT	Pelvic floor muscle training
PIM	Potentially inappropriate medicine
PIP	Potentially inappropriate prescribing
PMR	Patient medical record
PPO	Potential prescribing omission
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
RCT	Randomised control trial
SCH	Subclinical hypothyroidism
SPRM	Structured pharmacist review of medication
START	Screening tool to alert doctors to right treatment
STOPP	Screening tool of older persons prescriptions
STROBE	Strengthening the reporting of observational studies in epidemiology
TDF	Theoretical Domains Framework
TRUST	Thyroid Hormone Replacement for Subclinical Hypo-Thyroidism Trial
UCC	University College Cork
UK	United Kingdom
UI	Urinary incontinence
US	United States
VA	Veterans Affairs

Declaration

I declare that this thesis has not been submitted for another degree either at University College Cork or elsewhere. The work, upon which this thesis is based, was carried out in collaboration with a team of researchers and supervisors who are duly acknowledged in the text of the thesis. The Library may lend or copy this thesis upon request.

Signed: _____ Date: _____

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“Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young. The greatest thing in life is to keep your mind young.”

Henry Ford

Thesis Abstract

Background

Providing optimal care for older adults creates many challenges for healthcare providers especially general practitioners (GPs). Appropriate prescribing of medications is a significant challenge as older adults can present with multiple conditions for which multiple medications are often indicated. Potentially inappropriate prescribing (PIP) in older adults is common and is associated with negative health outcomes such as morbidity, adverse drug events, extended hospital stays and increased mortality. Therefore, the overarching aim of this thesis was to understand the potential role of the pharmacist in optimising prescribing for older people in primary care.

Methods

Multiple research methods were performed to address the thesis aim. A cross-sectional study was carried out to highlight the prevalence of prescribing issues in older adults across three countries. The published literature was then systematically reviewed to evaluate studies of pharmacist-led interventions on PIP among community-dwelling older adults in primary care to identify the components of a successful intervention. Based on the findings from the systematic review, a qualitative study was carried out to reveal the determinants of GP prescribing behaviour for older adults in primary care and to elicit GPs' views on the potential role for broad intervention strategies involving pharmacists and/or information technology systems in general practice. These findings then informed the pharmacist-led academic detailing intervention with GPs on the topic of urinary

incontinence in older people. This was a mixed methods feasibility study utilising qualitative focus groups with GPs and quantitative data from patient medical records in those ≥ 65 years with urinary incontinence in a region of Ireland.

Results

The cross-sectional study highlighted that the overall prevalence of PIP and potential prescribing omissions (PPOs) was 12.9% and 22.2% respectively in this cohort of European participants. The systematic review concluded that four out of the five studies included in the review were associated with an improvement in prescribing appropriateness. However it is unclear if these interventions result in clinically significant improvements in patient outcomes. The qualitative study highlighted the complexities of behavioural determinants of prescribing for older people in primary care and the need for additional supports for example, extra training in geriatric pharmacology and drug interactions to optimise prescribing for this growing cohort of patients. One approach that GP participants agreed could lead to a meaningful and sustained improvement in prescribing is interactive educational outreach or academic detailing. Therefore, an intervention was developed incorporating pharmacist-led academic detailing. In the feasibility study, the intervention was well received and highly valued by GPs. The measures of prescribing assessed before and after the intervention (LUTS-FORTA criteria; Drug Burden Index (DBI); Anticholinergic cognitive burden scale (ACB)); and the Screening Tool of Older Person's Prescriptions- Screening Tool to Alert Doctors to Right Treatment (STOPP/START) version 2 criteria) reported minimal or no change. However, as this was a feasibility study it was not designed or powered to demonstrate a change in these parameters.

Conclusion

This study has made an important contribution to the topic of prescribing for older adults in primary care by highlighting that educational interventions such as academic detailing are welcomed in the context of general practice in Ireland. The success of this educational strategy is likely to depend on engaging with all key stakeholders e.g. academic detailers, prescribers, professional bodies and academic institutions to ensure that the content delivered is relevant and practical to prescribers.

Chapter 1. Introduction

Population demographics are changing worldwide, with life expectancy and numbers of older persons increasing (1). In 1960, 8.6% of the Organisation for Economic Co-operation and Development (OECD) population was aged ≥ 65 years (2, 3). Today, that figure is 15.4% and by 2050 it is expected to rise to 27.2% (2, 3). In Ireland older individuals aged ≥ 65 years constitute approximately 12% of the population and it is estimated that by 2045 this figure will almost double. The proportion of individuals ≥ 85 years will almost triple during the same time period (4).

The ageing process is characterised by physiological changes that can influence the function of organ systems and compromise homeostatic capacity (5). Changes in body composition, hepatic and renal function can alter the volume of distribution of lipid soluble drugs, reduce the clearance of lipid and water soluble drugs, respectively. Pharmacodynamic changes can in general, increase the sensitivity to drugs (5). Additionally, older people are more likely to present with multiple conditions for which multiple medicines are required, increasing the probability of drug-drug and drug-disease interactions (6-9). Another major challenge is providing optimal care for older adults with multiple chronic conditions or “multimorbidity” (10-13). It is defined as the co-occurrence of two or more chronic conditions in a person (14). Multimorbidity is associated with many adverse outcomes including death, disability, increased burden of healthcare resources, negative impact on quality of life and a higher incidence of adverse effects to pharmacological or non-pharmacological interventions (10).

Therefore, providing optimal care for older adults creates many challenges for healthcare providers especially general practitioners (GPs) as they are the main prescribers of medication in primary care (11-13, 15).

1.1 Potentially inappropriate prescribing (PIP)

Medication related problems are common in older adults and are associated with increased morbidity, adverse drug events, adverse drug reactions, extended hospital stays and increased mortality (16-18). Potentially inappropriate prescribing (PIP) is a term used to describe a range of sub-optimal prescribing practices and can be classified as either:

- i. The prescribing of potentially inappropriate medicines (PIMs), the use of a medicine where no clear clinical indication exists or the use of a medicine in circumstances where the risks outweigh the benefits.
- ii. Potential prescribing omissions (PPOs), the under-prescribing of medicines for which there is a clear clinical indication (9).

PIP introduces the risk of an adverse drug event (ADE) which has the potential to outweigh the drug's clinical benefit, particularly when a safer or more effective alternative treatment option is available (19).

A number of studies have reported the prevalence of PIP/PPOs in large populations of older adults. Cahir *et al.* estimated the prevalence of PIP was 36% among adult's ≥70 years in a primary care population in Ireland (20). In a similar study, Bradley *et al.* reported a prevalence of PIP of 29% among older adults in primary care in the UK

(21). In the United States and Canada epidemiological studies have documented PIP prevalence rates in community-dwelling older adults ranging from 14% to 37% (22-24), while in Europe, PIP has been identified in 12-20% of older adults (25-27).

As older people have substantial variation in their health status for example, health, disease and disability, this makes the generalisation of prescribing decisions more challenging for prescribers (18). Limited availability and access to appropriate evidence based information in older and frail patients (studies have not been carried out, not synthesised or not available in the public domain) can also present challenges to healthcare providers (18, 28, 29). Despite the high prevalence of multimorbidity in the elderly population, most clinical trials focus on the benefit of one drug in one condition, thus excluding multimorbid participants (30, 31). These limitations cast doubt on otherwise high-quality clinical evidence, which in turn weakens prescribers' confidence in trial results (13). Therefore, interventions that optimise the quality of prescribing for this cohort of patients are necessary.

1.2. Methods to assess PIP

Assessing the appropriateness of prescribing in older people involves both implicit and explicit measures (20). Implicit measures involve a prescriber's judgment of appropriateness based on patient characteristics and published work (32). Explicit measures are criterion based and are derived from published literature, multidisciplinary expert panels and consensus validation methods (33).

The Medication Appropriateness Index (MAI) is an example of a validated implicit tool (34). It consists of ten criteria that relate to a number of different prescribing domains for example, indication, effectiveness, dose, duration, correct directions, practical directions, drug-drug interactions, drug-disease interactions, duplication and cost. The tool generates a weighted score (ranging from 0-18) per drug that serves as a measure of medication appropriateness. A higher score indicates an increased level of inappropriateness (34). The Assessment of Underutilization (AOU) is another implicit tool, however it only identifies prescribing omissions (35).

The first explicit tool for identifying PIP was the Beers criteria, developed in the United States in 1991 (19). The criteria were revised and updated in 1997, 2003, 2012 and 2015 (36). The Beers 2015 criteria are divided into five categories:

- i. Drugs to be avoided in older people independent of diagnoses.
- ii. Drugs to be avoided in older people with certain diseases and syndromes.
- iii. Drugs to be used with caution in older people.
- iv. Drugs to be avoided or have their dose adjusted, based on the individual's kidney function.
- v. Select drug-drug interactions documented to be associated with harm in older adults.

However, the Beers criteria contain several medicines that are either not prescribed or not available in most European drug formularies, thus its application in an EU setting is limited (37).

In recent years, the STOPP/START (Screening Tool of Older Persons Prescriptions, Screening Tool to Alert doctors to Right Treatment) criteria were developed and validated as an explicit measure of PIP and potential prescribing omissions (PPOs) for use in older adults (≥ 65 years) in European countries (38). The original STOPP set consisted of 65 criteria of PIP, including drug-drug and drug-disease interactions (potentially leading to side effects such as cognitive decline and falls in older people), as well as duplicate drug class prescriptions. The original START set consisted of 22 criteria that identify PPOs (38, 39). All criteria are organised according to physiological systems for ease of use (38). In 2014, due to an expanding therapeutics evidence base the STOPP/START criteria were revised and updated. A number of new evidence-based criteria were added and any obsolete or out of date criteria were removed. The revised set, STOPP/START version 2 (STOPP/START V2), consists of 80 STOPP and 34 START criteria. Several new STOPP categories created in version 2 include antiplatelet/anticoagulant drugs, drugs affecting, or affected by, renal function and drugs that increase anticholinergic burden. New START categories include urogenital system drugs, analgesics and vaccines (40).

Other explicit tools that have been developed worldwide include: the Australian Prescribing Indicators Tool which contains 45 explicit and 3 implicit prescribing indicators (41). The French Consensus Panel List contains 34 inappropriate practices in prescribing with recommendations for alternative therapies (42). The Improved Prescribing in the Elderly Tool (IPET) consists of 14 inappropriate practices in prescribing (43). The Norwegian General Practice Criteria (NORGEP) contains 36 criteria for pharmacologically inappropriate prescribing in general practice (44). The

PRISCUS list contains 83 drugs in a total of 18 drug classes as potentially inappropriate (45). The Thailand criteria consists of 77 practice statements or criteria for high-risk medication use (46). McLeod *et al.* developed a consensus-based list of 38 inappropriate high-risk practices in prescribing grouped into 4 categories with recommendations for alternative therapies (47). Zhan's criteria contains a classification of 33 drugs (48). The Zhan and McLeod criteria target older people ≥ 65 years, the IPET and NORGEF criteria focus on those ≥ 70 years, while the intended population for the French Consensus Panel list are those ≥ 75 years (42-44, 47, 48). There is no age stated for the Thailand criteria (46).

1.2.1. Other methods to optimise prescribing appropriateness

This section highlights a number of other criteria that focus on particular classes of medicines.

LUTS-FORTA criteria

Drugs to treat lower urinary tract symptoms (LUTS) regularly used in older people aged ≥ 65 years are classified on their appropriateness based on efficacy, safety and tolerability using the Fit fOR The Aged (FORTA) criteria. This validated criteria classifies drugs for the treatment of LUTS into four categories, A (absolutely: indispensable drug), B (beneficial: drugs with proven efficacy), C (careful: drugs with questionable efficacy/safety profiles) and D (don't: avoid in older people). Using a systematic approach including a literature search and a subsequent two-step Delphi process, an interdisciplinary international panel rated the appropriateness of the 16 most frequently prescribed drugs for the long term treatment of LUTS (49).

The Drug Burden Index (DBI)

The DBI was developed to measure the cumulative exposure to anticholinergic and sedative medicines in older people and its impact on physical and cognitive function (50). The calculation of the DBI is based on a pharmacological equation that incorporates drug dose and the principles of dose response (51).

$$DBI = \sum D / \delta + D$$

D is equal to the daily dose taken and δ is the minimum dose recommended by a relevant formulary (50). For each drug the DBI ranges from 0-1, with 0 being no burden, 0.5 being exposure to the minimum daily dose and upwards to 1 as the dose is increased exponentially (52). The sum of these individual drugs equals to the total drug burden.

Anticholinergic cognitive burden scale (ACB)

The cumulative effect of taking multiple medicines with anticholinergic properties is defined as the anticholinergic burden (53). Previous studies have demonstrated that the use of medicines with anticholinergic activity among older adults is associated with physical and cognitive decline (54, 55). The ACB is based on a systematic literature review of medicines with known anticholinergic activity. The scale assesses individual drugs that have none, possible or definite anticholinergic properties with a score ranging from 0 to 3 (56).

Several criteria e.g. STOPP/START, Beers, MAI have been developed to assess the prescribing appropriateness in older people. Application of such criteria may reduce

unnecessary use of medicines, adverse drug events, healthcare utilisation and economic burden (57). When selecting criteria for research purposes, it is important to consider the target population and clinical information available. Different tools can be used to optimise prescribing in older people, however, they are only intended to inform clinical judgment and not to replace it (58).

1.3 Interventions to optimise prescribing appropriateness

Interventions to optimise prescribing appropriateness in older adults have shown mixed results (59, 60). A number of strategies to address PIP are detailed in the following section.

1.3.1 Medication reviews

The overall aim of a medication review is to improve the quality, safety and appropriate use of prescribed medicines. Medication review is an overarching term which includes a number of interventions that may be carried out by the prescriber themselves (e.g. self-review by GPs, pharmacists or nurses) or by other healthcare professionals providing advice to prescribers (e.g. independent review carried out by pharmacists) (61). There is good evidence that medication reviews can improve prescribing outcomes including reduced polypharmacy, inappropriate prescribing and adverse drug effects (62, 63).

1.3.2 Computerised decision-support systems

Computerised decision support systems (CDSS) are widely used tools that optimise quality of care and patient outcomes (64). They are defined by Musen *et al.* as “any computer program designed to help healthcare professionals to make clinical decisions” (65). In practice these systems may involve an alert system appearing at the end of a consultation or at the time of prescribing (9, 38, 66).

These software systems have the potential to optimise prescribing appropriateness. A number of research projects are currently underway to assess prescribing appropriateness using CDSS. For example, a new Software Engine for the Assessment & Optimisation of drug and non-drug Therapy in Older peRsons (SENATOR) trial aims to optimise pharmacological and non-pharmacological therapy, and reduce the risk of adverse drug reactions (ADRs) in multimorbid hospitalised older adults. This randomised control trial (RCT) involves recruiting patients from six European hospital sites. The STOPP/START V2 criteria will be incorporated into the software engine and will form the basis of recommendations on optimal pharmacological therapy (<http://www.senator-project.eu/>). The OPERAM study (OPTimising thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly) aims to reduce the rates of over and under prescribing of medications among older European adults with multimorbidity. This large multicentre cluster randomised clinical trial will use a sophisticated software tool to determine if the intervention can improve clinical and economic outcomes for patients (67).

1.3.3 Academic detailing

Academic detailing (AD) or educational outreach is a form of continuing medical education (CME) in which a trained healthcare professional such as a pharmacist, nurse or doctor visits a prescriber in their practice environment to provide evidence-based information on a selected topic (68). These educational strategies which utilise interactive and tailored approaches with direct feedback have been shown to be effective at improving prescribing appropriateness (69). Several studies have also highlighted that GPs rate the educational value of AD highly (70, 71).

1.4 The role of the pharmacist in primary care in Ireland

Pharmacists play a vital role in the primary healthcare system. In Ireland, they are the most accessible healthcare professional, with approximately 2 million people visiting a pharmacy on a monthly basis, while 20 million prescriptions are filled in pharmacies annually (72). Therefore, pharmacists are ideally placed to support patients in maintaining and improving their health. Over the years, the role of the pharmacist in Ireland has changed significantly, with more pharmacists providing healthcare services such as administration of the flu vaccine, provision of emergency contraception, smoking cessation initiatives, cholesterol, diabetes and INR testing as well as dispensing medicines. These services can deliver significant benefits to both patients and the State by relieving the pressure from other areas of the healthcare system such as GPs and hospitals, allowing them to focus on more complex patients who require medical intervention (72).

1.5. Aim

The overall aim of this thesis is to understand the potential role of the pharmacist in optimising prescribing for older people in primary care.

1.6. Objectives

The specific objectives of the thesis are:

1. To estimate and compare the prevalence and type of PIP and PPOs amongst community-dwelling older adults (≥ 65 years) in three European populations. This sets the scene for the thesis by highlighting and comparing the prescribing issues for older adults across three populations.
2. To systematically review and summarise the literature on pharmacist-led interventions that optimise prescribing appropriateness among community-dwelling older adults receiving primary care to identify the components of a successful intervention.
3. To explore GPs' experiences of prescribing for patients ≥ 65 years and their views on the potential role for interventions involving pharmacists and/or information technology systems in general practice.
4. To evaluate the feasibility and satisfaction of a pharmacist-led academic detailing intervention with GPs in primary care.

1.7. Thesis Outline

This thesis contains seven chapters, four of which are studies that address the aims and objectives (Figure 1.1).

Chapter 2 gives an overview of the research methods used in this thesis. This chapter reviews and justifies the research methods which underpinned this doctoral research.

In **Chapter 3**, the prevalence and type of PIP and PPOs amongst community-dwelling older adults are compared across three European populations to highlight the complex nature of prescribing in this cohort of patients. A secondary analysis of the Thyroid Hormone Replacement for Subclinical Hypo-Thyroidism Trial (TRUST) dataset was carried out. A subset of 48/80 PIP and 22/34 PPOs indicators from the STOPP/START V2 criteria were applied to prescribed medication data for 532 out of 737 trial participants in Ireland, Switzerland and the Netherlands.

Chapter 4 systematically reviews the literature of pharmacist-led interventions that optimise prescribing appropriateness in community-dwelling older adults to identify components of a successful intervention. An electronic search of the literature was conducted using 11 databases. Studies were included if they were randomised controlled trials (RCTs) or quasi-randomised studies involving a pharmacist-led intervention compared to usual/routine care which aimed to reduce potentially inappropriate prescribing (PIP) in older adults in primary care.

Chapter 5 describes qualitative research on GPs' perspectives on prescribing for older people in primary care. Semi-structured qualitative interviews were carried out with a purposive sample of 16 GPs in County Cork, Ireland. Emerging themes were

mapped to the Theoretical Domains Framework (TDF), a tool used to apply behaviour change theories.

Chapter 6 is a feasibility study of a pharmacist-led intervention, which was conducted with GPs. This is a mixed methods feasibility study utilising data from qualitative focus groups with GPs and patient medical records in those ≥ 65 years with urinary incontinence in a region of Ireland. Qualitative focus groups were carried out with 14 GPs who participated in the AD intervention on urinary incontinence in older people. The focus groups were transcribed verbatim and analysed using thematic analysis. The medical records for all patients (154) aged ≥ 65 years who were attending a participating GP with a diagnosis of urinary incontinence were retrieved and analysed using a before-after approach. The measures of prescribing assessed before and after the AD intervention were: LUTS-FORTA criteria; Drug Burden Index; Anticholinergic cognitive burden scale; and the Screening tool of older person's prescriptions-screening tool to alert doctors to right treatment (STOPP/START) version 2 criteria.

Chapter 7 provides an overall discussion of the research, including strengths and limitations and makes suggestions for future research and policy implications.

Aim: To understand the potential role of the pharmacist in optimising prescribing for older people in primary care

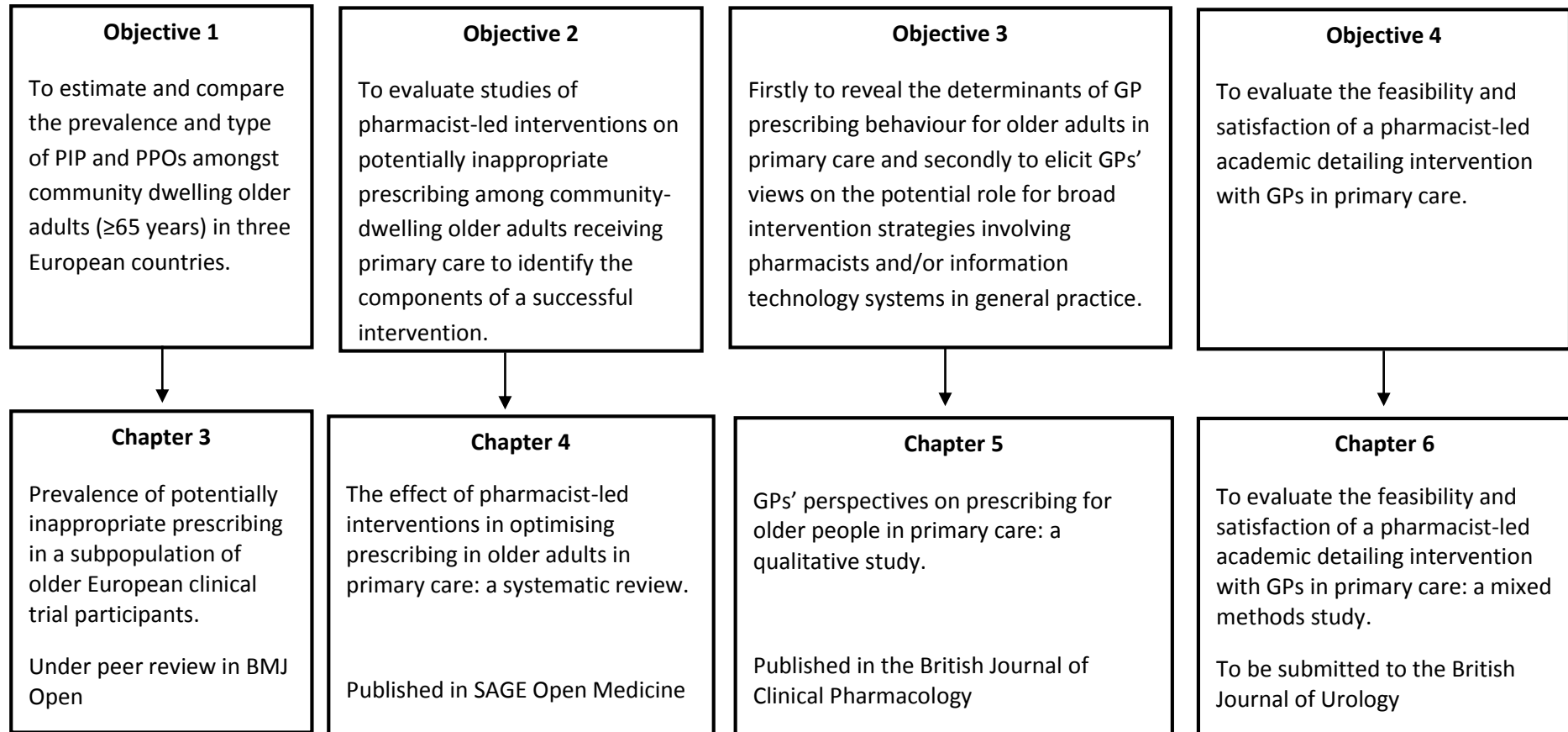


Figure 1.1 Thesis outline

1.8. Author's contribution to the included studies

I was the lead author of the research papers in Chapters 3 to 6. This involved the acquisition, analysis and interpretation of data for the study, the drafting and revising of each manuscript.

Additional expertise was gained from the following individuals:

- Dr Anthony Fitzgerald, School of Mathematical Sciences, UCC.
 - Expertise on regression analysis for the cross-sectional study (Chapter 3).
- Professor Patricia Kearney, Department of Epidemiology & Public Health, UCC.
 - Expertise on the study design and statistical analysis, for the cross-sectional study (Chapter 3).
- Professor Stephen Byrne, School of Pharmacy, UCC.
 - Expertise on study design and inclusion/exclusion criteria required for the systematic review (Chapter 4).
- Dr Paul Beirne, Department of Epidemiology and Public Health, UCC.
 - Expertise on the appropriate risk of bias tool for the systematic review (Chapter 4).

- Dr Rose Galvin, Department of Clinical Therapies, Health Research Institute, University of Limerick.
 - Expertise on evaluating the risk of bias for the included studies for the systematic review (Chapter 4).

- Mr Ben Meehan, QDATRAINING: NVivo Training, Consultancy & Support.
 - Expertise on the use of NVivo software for the qualitative study (Chapter 5).

- Dr Carol Sinnott, Department of Public Health and Primary Care, Cambridge Institute of Public Health, Cambridge, UK.
 - Expertise on the study design, sampling approach and data analysis for the qualitative study (Chapter 5).

- Dr Michael Fisher, Harvard Medical School, Boston, Massachusetts, USA.
 - Expertise on formulating the academic detailing intervention for the mixed methods study (Chapter 6).

- Professor Jerry Avorn, Harvard Medical School, Boston, Massachusetts, USA.
 - Expertise on formulating the academic detailing intervention and permission for use of the urinary incontinence educational materials for the mixed methods study (Chapter 6).

- Miss Eimir Hurley, Centre for Health Policy and Management, Trinity College Dublin.
 - Expertise on the design, implementation and evaluation of the academic detailing intervention, and facilitation of three focus groups for the mixed methods study (Chapter 6).

1.9 Publications

O' Riordan D, Walsh K, Galvin R, Sinnott C, Kearney P.M, Byrne S. The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review. *Sage Open Medicine*, May 2016.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4910534/>

O' Riordan D, Byrne S, Fleming A, Kearney P.M, Sinnott C. GPs' perspectives on prescribing for older people in primary care: a qualitative study. *British Journal of Clinical Pharmacology*, January 2017.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5465342/>

Walsh K, O' Riordan D, Kearney P.M, Timmons S, Byrne S. Improving the appropriateness of prescribing in older patients: a systematic review and meta-analysis of pharmacists' interventions in secondary care. *Age and Aging*, January 2016.

<https://www.ncbi.nlm.nih.gov/pubmed/26755524>

Stott D.J, Rodondi N, Kearney P.M, Ford I, Westendorp R.G.J, Mooijaart S.P, Sattar N, Aubert C.E, Aujesky D, Bauer D.C, Baumgartner C, Blum M.R, Browne J.P, Byrne S, Collet T.-H, Dekkers O.M, den Elzen W.P.J, Du Puy R.S, Ellis G, Feller M, Floriani C, Hendry K, Hurley C, Jukema J.W, Kean S, Kelly M, Krebs D, Langhorne P, McCarthy G, McCarthy V, McConnachie A, McDade M, Messow M, O'Flynn A, O'Riordan D, Poortvliet R.K.E, Quinn T.J, Russell A, Sinnott C, Smit J.W.A, Van Dorland H.A, Walsh K.A, Walsh E.K, Watt T, Wilson R, Gussekloo J. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. *New England Journal of Medicine*, March 2017.

<https://www.ncbi.nlm.nih.gov/pubmed/28402245>

1.10 Conferences attended

Date	Conference	Presentation title	Oral or Poster	Abstract published
Friday January 9th 2015	SPHeRE network 1 st Annual Conference – ‘Creating links for effective collaboration’, RCSI, Dublin.	Prevalence of potentially inappropriate prescribing (PIP) and potentially prescribing omissions (PPO) in older Irish adults: findings from a randomised placebo-controlled trial (TRUST).	Poster presentation	
Friday 23th January 2015	Prescribing and Research in Medicines Management (PRIMM) Conference, Imperial Hotel, London.	An evaluation of the reclassification of medicines from prescription only medicine (POM) to pharmacy supply (P) in Ireland.	Poster presentation	Journal of Pharmacoepidemiology and Drug Safety 15 June 2015.
Tuesday 27th January 2015	All Ireland Pharmacy Healthcare Conference, Ballymascanlon House Hotel, Dundalk.	Prevalence of potentially inappropriate prescribing (PIP) and potentially prescribing omissions (PPO) in older Irish adults: findings from a randomised placebo-controlled trial (TRUST).	Oral presentation	
Thursday 16th, Friday 17th April 2015	21 st Health Services Research and Pharmacy Practice (HSRPP) conference, Riddel Hall, Queens University Belfast.	Prevalence of potentially inappropriate prescribing (PIP) and potentially prescribing omissions (PPO) in older Irish adults: findings from a randomised placebo-controlled trial (TRUST).	Oral presentation	International Journal of Pharmacy Practice (IJPP) Vol 23, Supplement 1, April 2015.
Thursday 23rd- Sunday 26th April 2015	The International Association of Gerontology and Geriatrics-European Region (IAGG-ER) 8 th Congress, Dublin Convention Centre.	Prevalence of potentially inappropriate prescribing (PIP) and potentially prescribing omissions (PPO) in older Irish adults: findings from a randomised placebo-controlled trial (TRUST).	Poster presentation	
Monday 29th February 2016	2 nd Annual SPHeRE Network Conference - ‘Population health and health services research in Ireland: current trends and future directions’, RCSI College Hall, St Stephen’s Green, Dublin.	The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review.	Oral presentation	

Wednesday 6th- Friday 8th July 2016	45 th Annual Scientific Meeting of the Society for Academic Primary Care (SAPC), Dublin Castle.	GPs' perspectives on prescribing for older people in primary care: a qualitative study.	3min Elevator pitch	
Thursday 25th- Sunday 28th August 2016	32 nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management. Convention centre Dublin.	The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review.	Poster presentation	Journal of Pharmacoepidemiology and Drug Safety. Volume 25, Issue Supplement S3, August 2016, Pages 1–2.
Thursday 29th September – Saturday 1st October 2016	Irish Gerontological Society (IGS) 64 th Annual and Scientific Meeting, The Malton Hotel, Killarney, Ireland	GPs' perspectives on prescribing for older people in primary care: a qualitative study.	Poster presentation	Age & Ageing Volume 45, Number S2, September 2016.
Thursday 8th December 2016	3 rd New Horizons in Medical Research Conference, Main Atrium, Western Gateway Building, UCC, Cork.	The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review.	Poster presentation	
Thursday 12th January 2017	3 rd Annual SPHeRE Network Conference - 'Supporting Solutions: Connecting Research, Policy & Practice' RCSI College Hall, St Stephen's Green, Dublin.	Prevalence of potentially inappropriate prescribing in a sub-population of older European clinical trial participants.	Poster presentation	
Wednesday 22nd – Thursday 23rd February 2017	3 rd CBC Conference on Digital Health and Behaviour Change, Mary Ward House, Tavistock Place, London.	GPs' perspectives on prescribing for older people in primary care: a qualitative study.	Oral presentation	Frontiers Journal, 22 nd February 2017.
Monday 24th – Tuesday 25th April 2017	39 th All Ireland Schools of Pharmacy Conference, Cavanagh Pharmacy Building, University College Cork.	Prevalence of potentially inappropriate prescribing in a sub-population of older European clinical trial participants.	Poster presentation	

Chapter 2. Proposed stepped wedge trial design in primary care

This brief chapter describes an alternative intervention that was proposed for this thesis, however after some considerable discussion it was decided that it would not be feasible to carry out.

It consisted of a structured pharmacist review of medication (SPRM) with CDSS using STOPP/START V2 with feedback to GPs. This intervention was proposed for Mallow Primary Health Centre (MPHC), Mallow, County Cork. There are three GP practices that work independently of each other in MPHC with a total of 13 GPs (surgery 1: 6 GPs, surgery 2: 5 GPs, surgery 3: 2 GPs). The proposed intervention consisted of two components:

Intervention one: Structured pharmacist review of medication (SPRM) with CDSS using STOPP/START V2 with feedback to GPs.

Intervention two: Use of a CDSS by the GPs using STOPP/START V2.

The proposed method for carrying out this study was a stepped wedge randomised trial design. This involves sequential roll-out of an intervention to participants (either as individuals or clusters of individuals) over a number of time periods. By the end of the study, all participants receive the intervention, although the order in which participants receive the intervention is determined at random. Stepped wedge designs incorporate data collection at each point where a new group (step) receives the intervention. Data analysis to determine the overall effectiveness of the intervention subsequently involves comparison of the data points in the control section of the wedge with those in the intervention section (73).

Figure 2.1 shows the proposed stepped wedge trial design with the interventions rolled out over three time periods (T_0 , T_6 , T_{12} months). Firstly, a prevalence study of PIP & PPO using STOPP/START V2 was proposed to be carried at GP level (13 in total) in MPHC. Each surgery was due to be randomly assigned to an intervention (SPRM with CDSS using STOPP/START V2 with feedback to GPs, CDSS using STOPP/START V2 by GP or control). The aim of SPRM was to focus on medication optimisation which had the potential to identify and reduce ADRs. This was due be carried out by a research pharmacist (D.O.R.). MAI scores and prescribing patterns were due to be measured at baseline and at two subsequent six month intervals. The calculated MAI score in the control sections would then be compared with the intervention sections to assess prescribing appropriateness.

However, after discussing the proposed intervention with the IT software developer in MPHC it was suggested that this would not be feasible to carry out. This was primarily due to the cost of developing the CDSS software and compatibility issues with the GP software in the health centre. In MPHC, when the drug files are exported they are based on a comma delimited file, for example Amoxicillin 500mg tds is described as a “single word” i.e. “Amoxicillin500mgtds”. Also, these drug files are not linked to Anatomical Therapeutic Chemical (ATC) Classification System codes and are therefore not compatible with other software engines such as Software ENgine for the Assessment & optimization of drug and non-drug Therapy in Older peRsons (SENATOR) that are based on these codes. It was estimated that the cost of developing the software application would be between €10,000 and €25,000, however this was beyond the study budget. Therefore, developing an efficient

software engine to optimise drug therapy was going to be a significant challenge and as a result it was decided that a different intervention would have to be considered for the thesis.

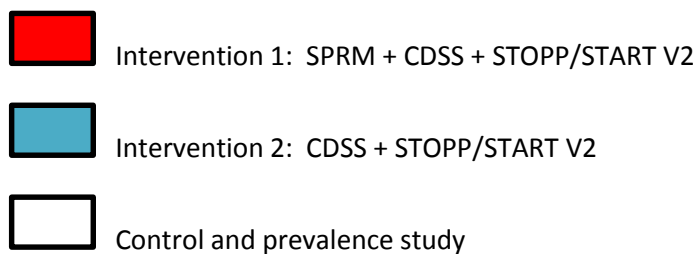
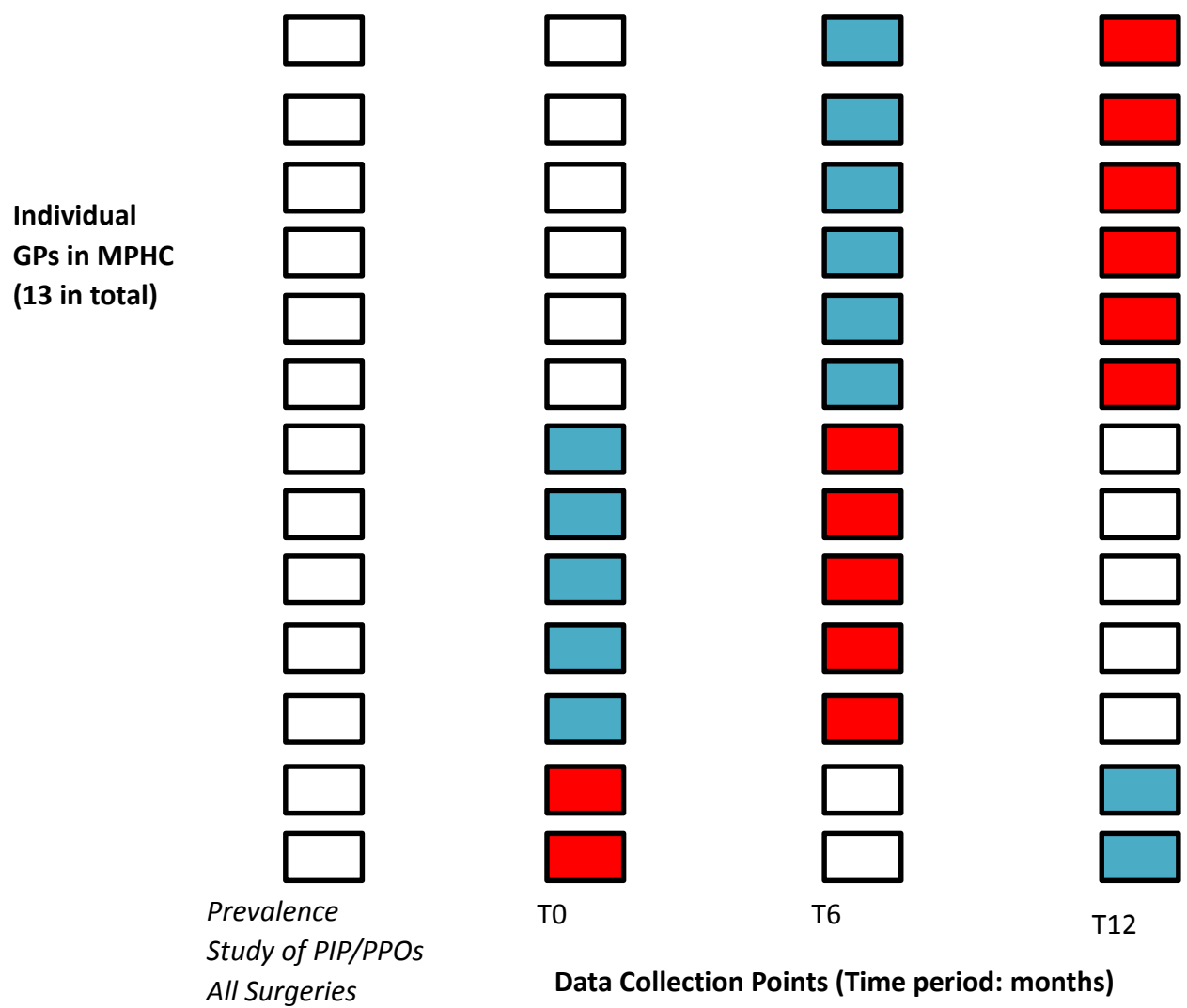


Figure 2.1 Stepped wedge design

Chapter 3. Prevalence of potentially inappropriate prescribing in a subpopulation of older European clinical trial participants

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This paper is under review in BMJ Open.

Abstract

Objectives

To estimate and compare the prevalence and type of potentially inappropriate prescribing (PIP) and potential prescribing omissions (PPOs) amongst community-dwelling older adults (≥ 65 years) enrolled to a clinical trial in three European countries.

Design

A secondary analysis of the Thyroid Hormone Replacement for Subclinical Hypothyroidism Trial (TRUST) dataset.

Participants

A subset of 48/80 PIP and 22/34 PPOs indicators from the STOPP/START V2 criteria were applied to prescribed medication data for 532/737 trial participants in Ireland, Switzerland and the Netherlands.

Results

The overall prevalence of PIP was lower in the Irish participants (8.7%), compared to the Swiss (16.7%) and Dutch (12.5%) participants ($p=0.15$) and was not statistically significant. The overall prevalence of PPOs was approximately one-quarter in the Swiss (25.3%) and Dutch (24%) participants and lower in the Irish (14%) participants ($p=0.04$) and the difference was statistically significant. The hypnotic Z-drugs were the most frequent PIP in Irish participants, (3.5%, $n=4$), while it was NSAID and oral anticoagulant combination, sulphonylureas with a long duration of action, and

benzodiazepines (all 4.3%, n=7) in Swiss, and benzodiazepines (7.1%, n=18) in Dutch participants. The most frequent PPOs in Irish participants were vitamin D and calcium in osteoporosis (3.5%, n=4). In the Swiss and Dutch participants, they were bone anti-resorptive/anabolic therapy in osteoporosis (9.9%, n=16; 8.6%, n=22) respectively. The odds of any PIP after adjusting for age, sex, multimorbidity and polypharmacy were ([aOR]) 3.04 (95% CI 1.33-6.95, p<0.01) for Swiss participants and aOR 1.74 (95% CI 0.79-3.85, p=0.17) for Dutch participants compared to Irish participants. The odds of any PPOs were aOR 2.48 (95% CI 1.27-4.85, p<0.01) for Swiss participants and aOR 2.10 (95% CI 1.11-3.96, p=0.02) for Dutch participants compared to Irish participants.

Conclusions

This study has estimated and compared the prevalence and type of PIP and PPOs among this cohort of community dwelling older people. It demonstrated a significant difference in the prevalence of PPOs between the three populations. Further research is urgently needed into the impact of system level factors as this has important implications for patient safety, healthcare provision and economic costs.

Keywords: Potentially inappropriate prescribing, Potential prescribing omissions, STOPP/START V2 criteria, European older adults.

Strengths and limitations of this study

- This is the first study to estimate and compare the prevalence and type of PIP and PPOs using a subset of the STOPP/START V2 criteria in community-dwelling older adults enrolled to a clinical trial across three different European countries.
- The TRUST database contains comprehensive information on patient demographics, co-morbidities and medication which facilitated the assessment and measurement of prescribing commission and omission for participants included in the clinical trial.
- The sample size (n=532) and sampling scheme may limit insights about prescribing nationally in the three countries.
- It was only possible to apply a subset of the criteria to the database due to a lack of information on drug strength, dose and duration of prescriptions and this may explain the low prevalence of PIP and PPOs in the study.
- Some countries may have specific guidelines for the optimal treatment of conditions, therefore these guidelines could differ from the recommendations in the STOPP/START criteria and could explain why some PIP and PPOs were identified in one population and not in others.

Introduction

Older people often have multiple comorbidities and as a consequence are frequently prescribed multiple drugs. This increases their risk of adverse drug events (ADEs), extended hospital stays and mortality (74). Potentially inappropriate prescribing (PIP) describes any drug that has the potential to cause an adverse event which can outweigh its clinical benefit when compared to alternative treatment options (19). Appropriateness of prescribing in older people can be assessed using either implicit (judgement-based) or explicit (criterion-based) screening tools (18). Implicit tools require healthcare professionals to assess the appropriateness of prescribing based on clinical guidelines and each patient situation (18). Explicit tools are usually developed from published literature, expert opinion and consensus techniques (75).

In recent years, the STOPP/START (Screening Tool of Older Persons Prescriptions, Screening Tool to Alert doctors to Right Treatment) criteria were developed and validated as an explicit measure of PIP and potential prescribing omissions (PPOs) for use in older adults (≥ 65 years) in European countries (76). The STOPP set consists of 65 criteria for PIP, including drug-drug and drug-disease interactions (potentially leading to side effects such as cognitive decline and falls in older people), as well as duplicate drug class prescriptions. The START set consists of 22 criteria that identify PPOs (39, 76). All criteria are organised according to physiological systems for ease of use (77). In 2014, the STOPP/START criteria were revised and adapted to new evidence-based guidelines. Twelve STOPP version 1 criteria were removed from version 2 because of weak or equivocal supporting evidence, while 27 new criteria were introduced in STOPP version 2. Three START version 1 criteria were removed

from version 2, while 15 new criteria were introduced. The revised set, STOPP/START version 2 (STOPP/START V2), consists of 80 STOPP and 34 START criteria. Several new STOPP categories created in version 2 include antiplatelet/anticoagulant drugs, drugs affecting, or affected by, renal function and drugs that increase anticholinergic burden. New START categories include urogenital system drugs, analgesics and vaccines (40). The effectiveness of the STOPP/START criteria in improving prescribing quality and clinical and economic outcomes has been shown in a recent systematic review (78).

A number of studies have reported the prevalence of PIP/PPOs in large populations of older adults using subsets of the STOPP/START V1 criteria. Cahir *et al.* estimated the prevalence of PIP was 36% among adults ≥ 70 years in a primary care population in Ireland (20). In a similar study, Bradley *et al.* reported a prevalence of PIP of 29% among older adults in primary care in the UK (21). However, there is a lack of research exploring the prevalence of PIP and PPOs in community-dwelling older adults using the updated criteria. Therefore, the aim of this study is to estimate and compare the prevalence and type of PIP and PPOs among a sample of community-dwelling older adults enrolled to a clinical trial across three different European countries using a subset of the STOPP/START V2 criteria.

Methods

Study population

This current study was a secondary analysis of the Thyroid Hormone Replacement for Subclinical Hypo-Thyroidism Trial (TRUST) dataset. The full study protocol for the TRUST trial has been previously published and a summary is provided here (79). The trial was conducted in four countries (Ireland, Scotland, Switzerland and the Netherlands). Community-dwelling participants aged ≥ 65 years with untreated subclinical hypothyroidism (SCH) were identified from clinical laboratory databases or by searching General Practitioners' (GP) databases/notes and were randomly assigned to levothyroxine or placebo. SCH was defined as persistently elevated thyroid stimulating hormone (TSH) levels (4.6-19.9 mU/L) with free thyroxine (fT4) within the local laboratory reference range (79, 80).

Medication information from the TRUST dataset was available for three of the four countries (Ireland, Switzerland [one site, Bern] and the Netherlands). On enrolment to the TRUST study in Ireland and the Netherlands, participants self-reported their prescription medicines and medical history to the study nurses. In Ireland, this involved participants bringing their medicines or prescription and a list of their medical conditions to the study visit. In the Netherlands, the study visit was carried out in the participant's home. In Switzerland, the study nurses received a list of the medical history and prescription medicines from the participant's GP. When it was not possible to obtain either list, the participants self-reported their medical history and prescription medicines. If ambiguity occurred regarding the reporting of prescription medicines or medical history in any of the study sites, the participant's

GP or local pharmacy were contacted. The study nurses recorded all the participants' prescribed medicines and entered them into an online electronic case report form (eCRF). Detailed information on participant demographics (date of birth, sex, race, smoking history, alcohol consumption), social circumstances (living arrangements, home support services, district nurse/public health nurse, informal caregiver), body measurements (systolic and diastolic blood pressure, heart rate, weight, height, waist circumference) and medical history were also collected. The data for this current study was obtained following access to the secure eCRF on the TRUST web portal (79).

Application of the STOPP/START criteria

There have been significant changes to the updated criteria. Firstly there are more criteria in V2 (80 STOPP and 34 START compared 65 STOPP and 22 START in V1). Secondly, new drug groups have been included in the updated criteria for example, sulphonylureas with a long duration of action. Thirdly, a number of criteria from V1 were removed from V2 due to a lack of evidence from the published literature. The extra criteria included in V2 arose from new clinical trial information, new systematic information and expert panel suggestions for new criteria. This highlights the need to update and revise the criteria on a regular basis as some criteria can become outdated or obsolete. Also, new drugs have entered the market since the V1 criteria were validated in 2008.

A subset of the STOPP/START V2 criteria were applied, as information required for some criteria (i.e. drug strength, dose and duration of prescriptions) was not available in the TRUST dataset. There was consensus among the study pharmacists (D.O.R., K.W. and S.B.) on the number and type of criteria selected, based on the ability to confidently apply the criteria to the data available. Therefore 48 PIP indicators and 22 PPOs indicators were applied (See Appendix I). Prescription drugs identified from the database were used as proxies to indicate a diagnosis of certain clinical conditions such as Parkinson's disease, glaucoma and gout. For example, if a participant was prescribed colchicine this information was used as a proxy for a diagnosis for gout. This methodology has been used in previous studies (57). A coding scheme was then developed between D.O.R. and K.W. PIP and PPOs prevalence were estimated according to STOPP/START V2 and recorded in Microsoft Office Excel[®] (2013). It was agreed *a priori* by the authors that D.O.R. (research pharmacist) would manually apply the criteria to all the Irish, Swiss and Dutch data. For validation purposes, the criteria were applied independently by a second member of the research team. K.W. (research pharmacist) applied the criteria to a random 10% sample of the Irish and Dutch data. C.E.A. (research medical doctor) applied the criteria to a random 10% sample of the Swiss data. There are two studies (OPERAM, SENATOR) currently assessing the automatisation of the STOPP/START criteria to identify PIP and PPOs in older people. The results from both studies should inform on the best method of automatizing screening tools to identify PIP and PPOs in this group of people. Therefore, the method used in this study for assessing the STOPP/START criteria should be considered as valid.

Outcomes

The main outcome of interest in this current study was the overall prevalence of any PIP or PPOs among participants from the TRUST trial in Ireland, Switzerland and the Netherlands according to a subset of the STOPP/START V2 criteria. Secondary outcome measures were: (1) the prevalence of PIP and PPOs for each individual STOPP/START V2 criterion (2) the most common PIP and PPOs in each country and (3) the association between the explanatory variables: country, age, sex, multimorbidity and polypharmacy and dependent variables: PIP and PPOs.

Statistical analysis

Data analyses were performed using STATA® version 13 (StataCorp, College Station, Tx, USA). Statistical significance was considered $p < 0.05$. Characteristics of included participants were stratified by country. Continuous variables were presented as mean with standard deviation (SD) and range, or median with interquartile range (IQR), as appropriate, and categorical variables as frequency (percentage). The overall prevalence of PIP/PPOs was defined as the proportion of participants having at least one PIP or PPO according to the STOPP/START V2 criteria among all participants included in this analysis and was further stratified by country. The prevalence estimates were compared using the χ^2 test. Participants were further classified by sex and age group (65–74 years, ≥ 75 years). Other explanatory variables included polypharmacy, defined as the concurrent use of five or more medications and multimorbidity (co-occurrence of three or more chronic conditions) (81). The association between age, sex, multimorbidity, polypharmacy and country with any PIP/PPOs (versus none) was assessed using multivariable logistic regression and

presented as adjusted odds ratios (aOR) with 95% confidence intervals (CI) and p-values. Multicollinearity between the independent variables polypharmacy and multimorbidity was assessed by calculating the variance inflation factor (VIF). Sensitivity analysis excluding criteria triggered by combination of more than one drug was also performed.

Standardised reporting guidelines

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) standardised reporting guidelines for cross-sectional studies have been followed to ensure the uniform conduct and reporting of the research (See Appendix I) (82).

Ethical approval

Ethical approval was received from the relevant ethics committees at each TRUST site (See Appendix IX).

Results

Population characteristics

The population characteristics of the 532 out of 737 included TRUST participants are detailed in Table 3.1. The mean age (\pm SD) of participants was 74.6 (5.9) in Ireland, 76.4 (5.9) in Switzerland and 76.1 (6.8) years in the Netherlands. The proportion of females varied across countries from 42.6% in Ireland and 46.3% in Switzerland to 65% in the Netherlands ($p < 0.01$). Hypertension (which was defined from participants' medical history) was the most common morbidity reported in each country (Ireland 65.2%, Switzerland 51.2%, the Netherlands 44.7%). The median number of drugs (IQR) prescribed to participants in each country was 4 (2, 6).

Table 3.1 Baseline characteristics

Population characteristics (n=532)	Ireland	Switzerland	Netherlands	P-values
Number of patients, n (% of total population in study)	115 (21.6)	162 (30.5)	255 (47.9)	
Mean age (years) (\pm SD), range	74.6 (5.9), 66-95	76.4 (5.9), 66-92	76.1 (6.8), 66-95	P= 0.054
Female, n (%)	49 (42.6)	75 (46.3)	166 (65.1)	P< 0.001
Current smokers, n (%)	5 (4.3)	12 (7.4)	24 (9.4)	P= 0.02
Mean alcohol consumption (units per week) (\pm SD)	5.5 (9.4)	3.6 (4.9)	7.4 (10.3)	P= 0.008
*Living arrangements (co-habiting), n (%)	77 (66.9)	91 (56.2)	161 (63.1)	P= 0.021
Mean BMI (\pm SD)	28.3 (4.3)	27.5 (4.9)	27.8 (4.8)	P= 0.318
Most common morbidity, Hypertension, n (%)	75 (65.2)	83 (51.2)	114 (44.7)	P= 0.001
Median number of drugs prescribed per patient, interquartile range (IQR)	4 (2,5)	4 (2,5)	4 (2,6)	P= 0.828
**Polypharmacy, n (%)	51 (44.3)	60 (37.0)	106 (41.6)	P= 0.447
Mean (\pm SD) EuroQoL 5D: EQ Visual Analogue Scale score/100	82 (15.2)	82 (12.1)	76 (11.6)	P<0.001
Mean (\pm SD) Mini-Mental State Examination (MMSE/30)	28 (2.2)	28 (1.8)	29 (1.2)	P< 0.001
Mean (\pm SD) ***TRUST Barthel Index/22	22 (1.0)	22 (1.0)	22 (1.0)	P= 0.010

* Living arrangements: Whether participants were co-habiting or living alone. ** Polypharmacy: defined as 5 or more regular medicines. ***An extra question was added under the heading "Bladder": "Does the participant have a urinary catheter?"

Overall prevalence of PIP and PPOs in each country

The overall prevalence of PIP in the three populations was 12.9% (n=69). It was lower in the Irish participants 8.7% (n=10) compared to the Swiss 16.7% (n=27) and Dutch 12.5% (n=32) participants (p=0.15). In Ireland, 7% (n=8) of participants had a single PIP compared to 13.6% (n=22) of participants in Switzerland and 11.8% (n=30) of participants in the Netherlands. In Ireland, 1.8% (n=2) of participants had two or more PIP compared to 3.1% (n=5) of participants in Switzerland and 0.8% (n=2) of participants in the Netherlands.

The overall prevalence of PPOs in the three populations was 22.2% (n=118). It was approximately one-quarter in the Swiss 25.3% (n=41) and Dutch 24% (n=61) participants and lower in the Irish 14% (n=16) participants (p=0.04). In Ireland, 12.0% (n=14) of participants presented with one PPO compared with 15.4% (n=25) of participants in Switzerland and 13.7% (n=35) of participants in the Netherlands. In Ireland, 1.7% (n=2) of participants presented with two or more PPOs compared with 9.9% (n=16) of participants in Switzerland and 10.2% (n=26) of participants in the Netherlands.

The most common PIP in each country

Figure 3.1 shows the most common PIP in each population. The hypnotic Z-drugs (zopiclone, zolpidem, zaleplon) were the most frequent PIP in Irish participants with 3.5% (n=4), followed by the prescribing of a beta blocker in participants diagnosed with bradycardia (< 50/min), type II heart block or complete heart block with 1.7% (n=2). The most frequent PIP in the Swiss participants were: 1) the combination of a non-steroidal anti-inflammatory drug (NSAID) with oral anticoagulants, (4.3%, n=7); 2) Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) in participants with type 2 diabetes mellitus, (4.3%, n=7); and 3) the prescribing of benzodiazepines, (4.3%, n=7). The most frequent PIP in the Dutch participants was the prescribing of benzodiazepines, (7.1%, n=18), followed by sulphonylureas with a long duration of action in participants with type 2 diabetes mellitus, (2.4%, n=6).

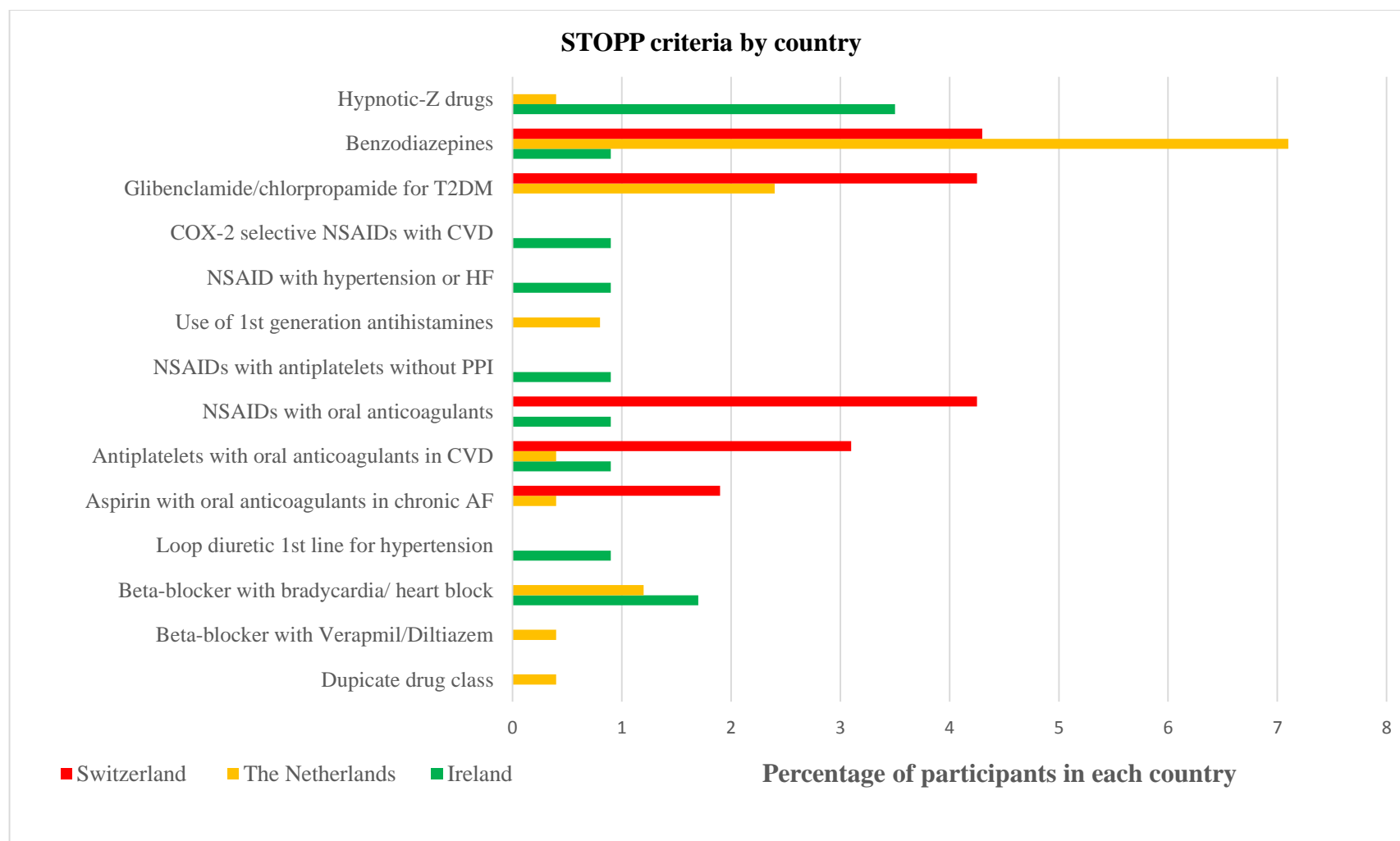


Figure 3.1 The most common types of PIP in each country.

Abbreviations: T2DM, Type 2 diabetes mellitus; COX, Cyclo-oxygenase; NSAID, Non-steroidal anti-inflammatory drug; CVD, Cardiovascular disease; HF, Heart failure; PPI, Proton pump inhibitor; AF, Atrial fibrillation.

The most common PPOs in each country

Figure 3.2 shows the most common PPOs in each population. The most frequent PPOs in Irish participants were vitamin D and calcium supplements in participants with known osteoporosis and/or previous fragility fracture(s), 3.5% (n=4). The second most frequent PPOs were regular inhaled β_2 agonists or antimuscarinic bronchodilators for mild to moderate asthma or COPD, 2.6% (n=3). The most frequent PPOs in the Swiss participants were bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in participants with documented osteoporosis, 9.9% (n=16). The second most frequent PPOs in the Swiss participants were antiplatelet therapy with a documented history of coronary, cerebral or peripheral vascular disease, 7.4% (n=12). The most frequent PPOs in the Dutch participants were bone anti-resorptive or anabolic therapy in participants with documented osteoporosis, 8.6% (n=22), followed by prescribing omissions of vitamin D and calcium supplement in participants with known osteoporosis and/or previous fragility fracture(s), 6.3% (n=16).

Factors associated with PIP

Table 3.2 shows the univariable and multivariable logistic regression analysis for the association between age, sex, comorbidities and polypharmacy with PIP. In the univariable and multivariable models, there was no statistically significant association between age or sex and PIP. However, the association between comorbidities or polypharmacy and PIP was statistically significant for both models.

Further analysis demonstrated that the odds of any PIP after adjusting for age, sex, multimorbidity and polypharmacy were (adjusted odds ratio) (aOR) 3.04, [(95% CI)

1.33-6.95, $p < 0.01$] for Swiss participants and aOR 1.74, [(95% CI) 0.79-3.85, $p = 0.17$], for Dutch participants compared to Irish participants.

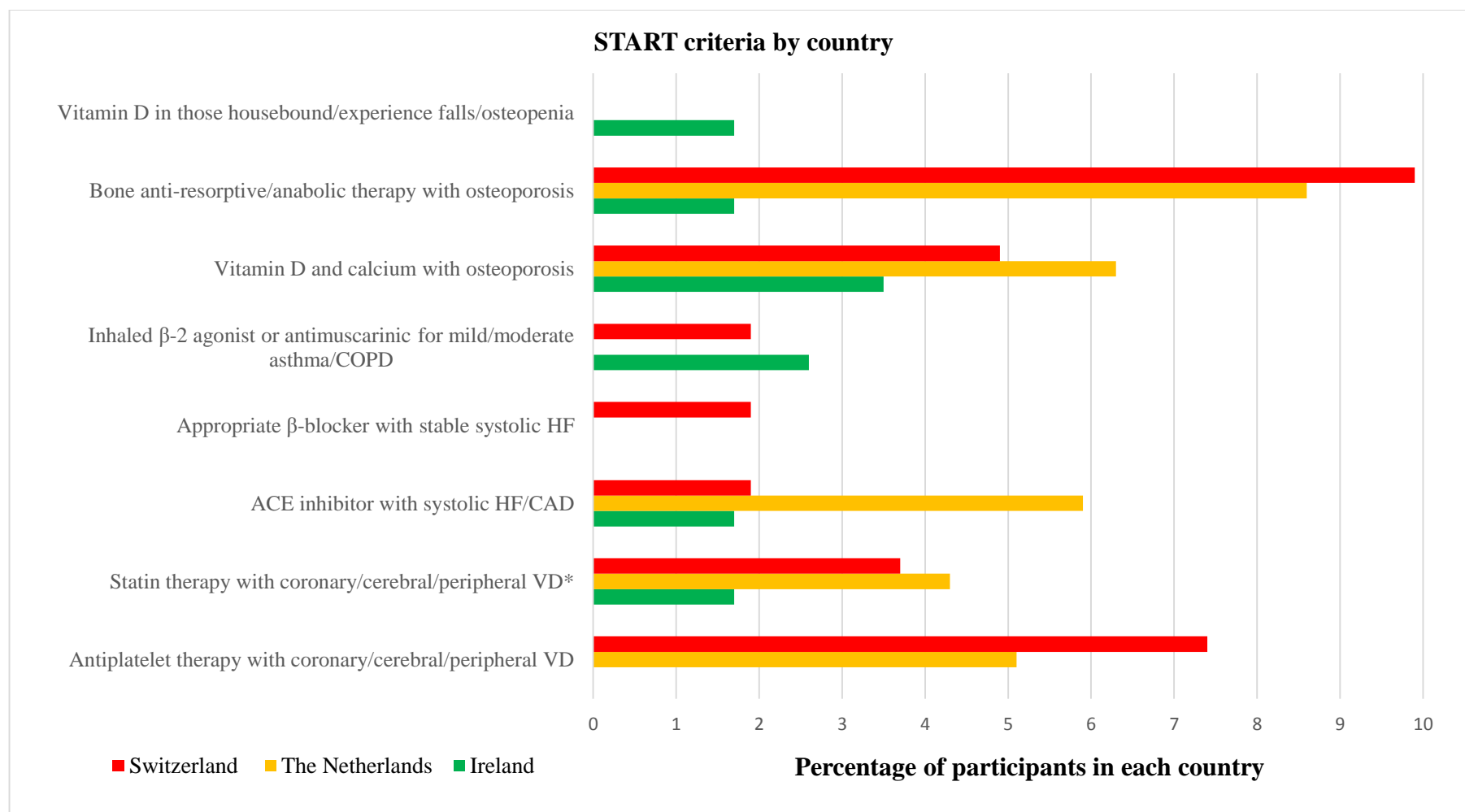


Figure 3.2 The most common types of PPOs in each country.

Abbreviations: ACE, Angiotensin converting enzyme; COPD, Chronic obstructive pulmonary disease; HF, Heart failure; CAD, Coronary artery disease; VD, Vascular disease; * Unless the patient's status is end-of-life or age is > 85 years

Table 3.2 Results of the univariable and multivariable logistic regression analyses for the association between age, sex, multimorbidity and polypharmacy with potentially inappropriate prescribing (PIP).

	Univariable model		Multivariable model*	
Explanatory variable	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Age (years)	1.02 (0.99-1.06)	0.22	0.99 (0.94-1.03)	0.54
Female (vs. male)	1.18 (0.70-1.96)	0.54	1.47 (0.84-2.59)	0.18
**Multimorbidity	3.24 (1.93-5.44)	<0.01	2.08 (1.16-3.73)	<0.01
***Polypharmacy	5.52 (3.10-9.86)	<0.01	4.81 (2.52-9.16)	<0.01

*Adjusted for age, sex, multimorbidity, polypharmacy and country. **Multimorbidity: defined as the co-occurrence of 3 or more chronic conditions. ***Polypharmacy: defined as 5 or more regular medicines.

Factors associated with PPOs

Table 3.3 shows the univariable and multivariable logistic regression analysis for the association between age, sex, multimorbidity and polypharmacy with PPOs. In the univariable model the association between age or multimorbidity and PPOs was statistically significant. However, the association was not statistically significant for sex or polypharmacy. In the multivariable model the association between sex or multimorbidity or age and PPOs was statistically significant. However, the association was not statistically significant for polypharmacy.

The odds of any PPOs after adjusting for age, sex, multimorbidity and polypharmacy were aOR 2.48, [(95% CI) 1.27-4.85, $p < 0.01$] for Swiss participants and aOR 2.10, [(95% CI) 1.11-3.96, $p = 0.02$] for Dutch participants compared to Irish participants.

The VIF for multimorbidity and polypharmacy were 1.82 and 2.13 respectively. Sensitivity analysis excluding criteria triggered by combination of more than one drug had no effect on the study results.

Table 3.3 Results of the univariable and multivariable logistic regression analyses for the association between age, sex, multimorbidity and polypharmacy with potential prescribing omissions (PPOs).

	Univariable model		Multivariable model*	
Explanatory variable	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Age (years)	1.04 (1.01-1.08)	<0.01	1.04 (1.00-1.07)	0.05
Female (vs. male)	1.41 (0.93-2.14)	0.11	1.63 (1.04-2.57)	0.04
**Multimorbidity	3.04 (1.99-4.65)	<0.01	4.01 (2.43-6.63)	<0.01
***Polypharmacy	1.30 (0.86-1.96)	0.21	0.69 (0.42-1.14)	0.144

*Adjusted for age, sex, multimorbidity, polypharmacy and country. **Multimorbidity: defined as the co-occurrence of 3 or more chronic conditions. ***Polypharmacy: defined as 5 or more regular medicines.

Discussion

Statement of principal findings

In this study across three European populations in adults aged 65 years or older, the overall prevalence of PIP was 12.9% (n=69) and was similar in the Irish, Swiss and Dutch participants. The overall prevalence of PPOs in the three populations was 22.2% (n=118) and was higher in the Swiss and Dutch than in the Irish participants. Participants at the Swiss and Dutch sites were at increased odds of any PIP and PPOs after adjusting for age, sex, comorbidities and polypharmacy compared to participants at the Irish site.

Results in the context of the current literature

A systematic review of thirteen research studies described the application of the STOPP/START V1 criteria in different healthcare settings. The prevalence of PIP and PPOs ranged from 21% to 79% and 23% to 74%, respectively (83). Studies reporting the prevalence of PIP and PPOs using the expanded STOPP/START V2 criteria in large populations of older people are limited. One study of 225 community-dwelling adults aged ≥ 65 years in Spain found an overall prevalence of PIP and PPOs of 40.4% and 21.8%, respectively (84). In a study conducted in Turkey, 667 participants aged ≥ 65 years were admitted to an outpatient clinic of a university hospital. The prevalence of PIP reported was 39.1% (85). A study conducted among 319 older patients discharged from a hospital in Albania identified that 63% received at least one PIP (86). In another study carried out in Ethiopia, the prevalence of inappropriate prescribing of antithrombotic therapy among 156 hospitalised elderly patients was assessed. The prevalence of PIP and PPOs were 51.4% and 48.6% respectively (87).

The overall prevalence of PIP and PPOs in this current study was lower compared to these studies. However, this may have been due to differences in number and type of criteria applied to the data.

In this study, the prescribing of benzodiazepines was identified as a common PIP among Dutch (7.1%, n=18) and Swiss participants (4.32%, n=7). However, in Ireland, it was reported at less than 1% (n=1). These findings are in keeping with a recent panel survey in Ireland using patient-level dispensing data, which highlighted that benzodiazepines were one of the few medicines without a yearly increase in prescribing between 1997 and 2012 (88). In 2009 a nationwide program was introduced in the Netherlands which aimed to reduce the prescribing rates of benzodiazepines. Dutch GPs are required to state the indication for all benzodiazepines prescribed to allow patients apply for reimbursement of the medicine costs (89). In Switzerland, no similar program exists. In Ireland, GPs receive a printout of their benzodiazepine prescribing from the General Medical Scheme (GMS). The GMS is a national tax-funded health insurance program that provides access to medical and surgical services for low income individuals/families and older people (89). This feedback highlights the prescribing practice of the GPs compared to their peers and allows them to carry out a clinical audit in this topic area. The audit also provides GPs with the necessary tools to identify best practice and this may have impacted on the low prescribing of benzodiazepines in this study, when compared with the two other countries. This low prevalence could also be due to a difference in the sampling approach in Ireland or it may have occurred by chance.

Frequent PPOs across all three populations in this study included vitamin D and calcium supplements in participants with known osteoporosis and/or fractures. These findings are similar to a previous study that used STOPP/START V1 criteria in a primary care setting in Ireland (37). Prescribing of proton pump inhibitors (PPIs) at full therapeutic dose for more than eight weeks is one of the most common STOPP criteria reported in studies but was not reported in this study as information relating to drug duration was not available (21, 88).

The screening process and identification of potential participants for this clinical trial differed between countries and may explain some of the differences in the prevalence of PIP and PPOs. In Ireland, clinical trial nurses visited individual GP surgeries and with GP approval performed a search of the GPs' databases/notes to identify potentially eligible participants. The GP then confirmed whether the participant was eligible to participate in a screening visit. In Switzerland and the Netherlands, potential participants were identified directly from clinical laboratory databases. A list of potential participants was sent to their GPs to confirm their eligibility in the trial. This screening process was carried out twice by the GPs and those who were deemed eligible were invited to participate (79). This process may have introduced selection bias at GP level as only GPs interested in participating in a clinical trial facilitated recruitment and also at the patient level as GPs may have excluded more complex patients. Furthermore, in Ireland and the Netherlands, GPs are gatekeepers of referral to specialist services (90, 91). Whereas in Switzerland, participants can visit medical specialists directly if necessary (91). A systematic review and meta-ethnographic synthesis of GPs' experiences on the clinical

management of multimorbidity identified “Disorganisation and fragmentation of healthcare” as a key difficulty. The authors highlighted that GPs have a more holistic view of the patient in contrast to specialists who manage disease specific conditions (92). As Swiss patients can visit medical specialists directly if necessary they may receive more non-essential medicines. The prescribing process is further complicated if patients attend several specialists. Also, if there is a lack of collaborative decision making between the patients’ GP and medical specialists this could result in a higher prevalence of PIP/PPOs among Swiss participants. Therefore, enhancing collaborative decision-making between GPs and specialists may help to optimise the prescribing of older patients. Finally, some countries may have specific guidelines for the optimal treatment of conditions. These guidelines could differ from the recommendations in the STOPP/START criteria and could explain why some PIP and PPOs were identified in one population and not in others.

Clinical and policy implications

The study findings indicate that the overall prevalence of PIP using a subset of the STOPP/START V2 criteria across three European populations was 12.9%. As PIP is associated with adverse health outcomes, healthcare providers should aim to reduce their prevalence (93, 94). A recent systematic review of 12 randomised controlled trials concluded that various interventions including pharmacist interventions, clinical decision support systems and multifaceted approaches can reduce inappropriate prescribing (60). However, it was unclear whether these interventions led to clinically significant improvements in patient outcomes due to the variability in methodological quality of the included studies and the heterogeneity of the

interventions and outcomes measured (60). Further large randomised controlled trials that are methodologically robust, adhere to the appropriate reporting guidelines, and have a long duration of follow-up are needed to address the efficiency of such interventions to reduce the prevalence of PIP/PPOs and improve patient outcomes. Despite the high prevalence of multimorbidity in the elderly population, most clinical trials focus on the benefit of one drug in one condition, thus excluding multimorbid participants (30, 31). These limitations cast doubt on otherwise high-quality clinical evidence, which in turn weakens prescribers' confidence in trial results (13). A number of prescribed drugs can be used as a proxy measure of multimorbidity in primary care (95, 96). Therefore, recruiting participants with higher levels of polypharmacy is one approach to help build an evidence base that is relevant to the majority of older people with multiple chronic conditions (97). For example, the OPERAM study (Optimising thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly) aims to reduce the rates of over- and underprescribing of medications among older European adults with multimorbidity. This large multicentre randomised clinical trial will use a sophisticated software tool to determine if the intervention can improve clinical and economic outcomes. The TRUST trial succeeded in recruiting participants with multimorbidity and polypharmacy by using a broad inclusion criteria and recruiting from primary care (80).

The potential role for medication reviews incorporating explicit screening tools of PIP for participants recruited to clinical trials requires further investigation. This may provide trialists with important information on the complex nature of prescribing

medication regimens in such participants, and how new interventions are expected to perform alongside these regimens. In addition, the cost of conducting these interventions in clinical trial participants should also be explored. Finally, screening tools such as the STOPP/START criteria have proven to be very beneficial not only in identifying the prevalence of PIP/PPOs in studies but also in intervention studies to improve medication appropriateness and reduce the risk of ADRs in older people (98). The updated version with the additional criteria will help to identify a larger number of PIP and PPO instances and therefore has a greater potential to reduce ADRs and improve other relevant patient outcomes.

Strengths and limitations of the study

To the best of our knowledge, this is the first study to estimate and compare the prevalence and type of PIP and PPOs using a subset of the STOPP/START V2 criteria in community-dwelling older adults across three different European populations. It also offered an opportunity to compare the characteristics of trial participants recruited by sites in different countries and to compare prescribing behaviours internationally. International comparisons can support or refute arguments for change in healthcare, serve as an additional lens on the state of the quality of care provided nationally, and can help build the evidence base necessary to identify problems and understand changes in the quality of care between countries. The TRUST database contains comprehensive information on patient demographics, co-morbidities and medication. This facilitated the assessment and measurement of prescribing commission and omission for participants randomised to the clinical trial. A number of different approaches for optimising prescribing appropriateness have

been published. For example, comprehensive geriatric assessment (CGA) is a time consuming and resource intensive strategy to deploy and is more commonly used for intervention rather than prevalence studies (9). Therefore, STOPP/START was considered the most appropriate and feasible tool for this study. The STOPP/START V2 criteria were applied by a pharmacist (D.O.R.) who is familiar with using this screening tool. To enhance the validity of the results, a sample of the data were independently reviewed by two health care professionals. It was agreed *a priori* to perform the multivariable analysis at the level of the patient rather than individual drug as the aim of the study was to estimate and compare the prevalence and type of PIP and PPOs in the study population.

It is acknowledged that the sample size (n=532) is relatively small, however, the aim was to estimate and compare the prevalence and type of PIP and PPOs in a sample of patients from three different European countries. The study population was based on participants enrolled to a clinical trial and may be somewhat different from the general population. However, the main inclusion criteria for the TRUST trial are quite broad. Secondly, although the data is based on a population of patients with SCH, there is no evidence to suggest that this would influence their chance of having a PIP or PPO. Although different approaches to the collection of medication data were used in each country, the authors (and the TRUST consortium with regards to safety) believe that all methods are thorough enough to capture all medication. For example, studies have highlighted that self-report medications are most likely to be congruent with patient records as a measure of current medications (99). It was only possible to apply a subset of the STOPP/START V2 criteria, as information required

for some criteria (i.e. drug strength, dose and duration of prescriptions) was not available in the TRUST dataset. For example, the prescribing of PPIs at full therapeutic dose for more than eight weeks was not reported. This may have contributed to an underestimation of the real prevalence of PIP in the study. Also, some of the criteria could be more explicit. For example, the C1 STOPP criterion “long term aspirin at doses greater than 160mg per day” does not define “long term”. This requires further clarification in future versions of the criteria (100). Although prescription drugs were used as proxies to indicate diagnoses, the possibility that these drugs may have been used to treat other conditions cannot be excluded. Finally, the TRUST trial concerned patients with subclinical hypothyroidism (SCH). It is possible that women with SCH were more likely than men to have been treated by doctors and therefore not eligible for the trial, as doctors tend to associate thyroid disease more with women. Also, SCH symptoms can overlap with post-menopausal symptoms that women report (i.e. tiredness, low mood etc.) therefore pushing doctors to treat this condition.

Conclusions

These study findings highlight that PIP and PPOs are prevalent among a sample of community-dwelling older people enrolled to a clinical trial in three European countries. The screening process and identification of potential participants for this clinical trial differed between the countries and may explain some variation in the populations recruited and prevalence of PIP and PPOs. This study is an important first step to justify the need for large comparative studies using routine data. This can then help to inform policy or the development of appropriate interventions on optimising prescribing practices in older adults at a national or international level. Further research is urgently needed into the impact of system level factors as this has important implications for patient safety, healthcare provision and economic costs.

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Chapter 4. The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review.

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Abstract**Objective:**

To evaluate studies of pharmacist-led interventions on potentially inappropriate prescribing among community-dwelling older adults receiving primary care to identify the components of a successful intervention.

Data Sources:

An electronic search of the literature was conducted using the following databases from inception to December 2015: PubMed, EMBASE, CINAHL, MEDLINE (through OVID), TRIP, Centre for Reviews and Dissemination databases, Cochrane Database of Systematic Reviews, ISI Web of Science, Science Direct, ClinicalTrials.gov, metaRegister of Controlled Trials (mRCT), ProQuest Dissertation and Theses Database, (Theses in Great Britain, Ireland and North America).

Review Methods:

Studies were included if they were randomised controlled trials (RCTs) or quasi-randomised studies involving a pharmacist-led intervention compared to usual/routine care which aimed to reduce potentially inappropriate prescribing (PIP) in older adults in primary care. Methodological quality of the included studies was independently assessed.

Results:

A comprehensive literature search was conducted which identified 2,193 studies following removal of duplicates. Five studies met the inclusion criteria. Four studies involved a pharmacist conducting a medication review and providing feedback to

patients or their family physician. One RCT evaluated the effect of a computerised tool that alerted pharmacists when elderly patients were newly prescribed potentially inappropriate medications. Four studies were associated with an improvement in prescribing appropriateness.

Conclusion:

Overall, this review demonstrates that pharmacist-led interventions may improve prescribing appropriateness in community-dwelling older adults. However, the quality of evidence is low. The role of a pharmacist working as part of a multidisciplinary primary care team requires further investigation to optimise prescribing in this group of patients.

Introduction

Medication related problems are common in older adults and are associated with increased morbidity, adverse drug events, extended hospital stays and increased mortality (16, 17, 101). Potentially inappropriate prescribing (PIP) can introduce the risk of an adverse drug event (ADE) which has the potential to outweigh the drug's clinical benefit, particularly when a safer or more effective alternative treatment option is available (19). The term "potentially" is used, as the physician may have considered the potential negative consequences of prescribing the drug as well as alternative treatment options for that patient but chose to proceed with a given approach (102). Recent evidence indicates that the prevalence of PIP in older adults in primary care is high, with nationally representative estimates in Ireland, Northern Ireland and the UK at 36%, 34% and 29% respectively using an explicit measure of inappropriate prescribing (103-105). Curtis *et al.* conducted a retrospective cohort study using a national sample of prescription drug claims for patients over 65 enrolled with a pharmaceutical benefit manager in the United States. The study highlighted that more than one in five patients filled a prescription for one or more drugs of concern based on the Beers revised list of drugs to be avoided in elderly populations (106).

A number of screening tools have been developed to assess the appropriateness of prescribing, which use an explicit (criterion-based) or implicit (judgement-based) approach (107). Explicit tools are usually developed from published literature, multidisciplinary expert panels and consensus validation methods. The potential drawbacks of using explicit criteria include a lack of transparency of the literature

used, reliability of the consensus techniques and conflicts of interest of the expert panels (33). Explicit criteria include the Beers and STOPP/START (Screening Tool of Older Persons Prescriptions, Screening Tool to Alert doctors to Right Treatment) criteria (19, 38). Beers criteria contain several medicines that are either not prescribed or not available in most European drug formularies, thus its application in an EU setting is limited (108). The STOPP criteria comprise a physiological systems based screening tool designed for use in Europe. It aims to identify potentially inappropriate medicines (PIMs) by listing explicit rules for avoidance of particular medicines in older people. In addition, potential prescribing omissions (PPOs) have been identified by an accompanying screening tool known as START (57).

In implicit approaches, healthcare professionals use information from the patient and published reviews to assess the appropriateness of medicines (18, 109). The Medication Appropriateness Index (MAI) is an example of a validated implicit tool (110). It consists of ten criteria that relate to a number of different prescribing domains for example, indication, effectiveness, dose, duration, correct directions, practical directions, drug-drug interactions, drug-disease interactions, duplication and cost. The tool generates a weighted score (ranging from 0-18) per drug that serves as a measure of medication appropriateness. A higher score indicates an increased level of inappropriateness (110). The application of implicit tools is time-consuming, depends on the users knowledge and in addition the MAI does not address under prescribing (107).

Across transitions of care, evidence indicates that pharmacists play a significant role in gate-keeping medication appropriateness, with respect to quality and safety of

prescribing (111). Research suggests that pharmacists can reduce PIP and adverse health outcomes in patients across a range of healthcare settings by utilising explicit and implicit screening tools systematically (112-115).

To date, evidence has been collated on various pharmacist-led interventions to reduce PIP across healthcare settings. However, no review has summarised the totality of evidence regarding the impact of pharmacist-led interventions to reduce PIP in older adults specifically in primary care.

Therefore, the aim of this review is to evaluate studies of pharmacist-led interventions on medication prescribing among community-dwelling older adults receiving primary care to identify the components of a successful intervention.

Methods

Standardised reporting guidelines

This systematic review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews And Meta-Analysis) standardised reporting guidelines to ensure the standardised conduct and reporting of the research (116). (See Appendix II)

Study identification

An electronic search of the literature was conducted using the following databases from inception to December 2015: PubMed, EMBASE, CINAHL, MEDLINE (through OVID), TRIP, Centre for Reviews and Dissemination databases, Cochrane Database of Systematic Reviews, ISI Web of Science, Science Direct, ClinialTrials.gov, metaRegister of Controlled Trials (mRCT), ProQuest Dissertation and Theses

Database, (Theses in Great Britain, Ireland and North America). A combination of the following keywords and MeSH terms were used: “primary care” or “primary health care” or “outpatient care” AND “prescribing” or “prescription” AND “aged” or “middle aged” or “elderly” AND “pharmacist” or “pharmaceutical care”. There were no date or language restrictions on the searches. A list of the search strategies for each database is provided in Appendix II. The references of final search results were hand-searched along with hand-searching the references of some already published reviews and the authors own records (112, 117).

Study selection

Studies were included if they met the following inclusion criteria: *Study design*; All randomised (cluster) controlled trials (RCTs), quasi RCTs, controlled before and after studies and interrupted time series designs (ITS) were included. *Population*; Community-dwelling older adult’s ≥ 65 years. Studies based on nursing home populations were excluded. A recent Cochrane review published by Alldred *et al.* (2016) focused on interventions to optimise prescribing for older patients in care homes. Eight out of the twelve studies retrieved were pharmacist-led (114). Therefore, it was decided that this question had already been answered for patients in this particular setting. *Intervention*; Pharmacist-led interventions were defined as any intervention where the pharmacist had the lead role in an intervention designed to reduce potentially inappropriate prescribing (PIP)/improve medication appropriateness in primary care. The *comparison* group were usual care or other active interventions not focused on medication appropriateness. *Outcome*; The primary outcome measure was the change in prescribing appropriateness using a

validated explicit or implicit screening tool for the detection of PIP i.e. Beers criteria, STOPP/START, MAI. Secondary outcomes included any clinical or patient self-reported outcomes (e.g. quality of life, patient satisfaction).

Studies were excluded if they were: currently ongoing; if there was a lack of reply from the author for supplementary information and if they only carried out an economic analysis. A list of the excluded studies reviewed with reasons for exclusion is provided in Appendix II.

Study selection and data extraction

Two reviewers (D.O.R. and K.W.) independently read the titles and/or abstracts of the identified papers and eliminated irrelevant studies. Studies considered to be eligible for inclusion were read in full and their suitability for inclusion was determined independently by two reviewers (D.O.R., K.W.). Disagreements were managed by consensus. However, if this was not successful, consensus was sought by a third reviewer (S.B.).

Data were extracted using an extraction form created on Microsoft Excel, based on study design and setting, patient demographics and inclusion criteria, details of the intervention and comparison, length of follow-up and outcome measures used. Authors were contacted to provide supplementary information when insufficient data were provided in the study. The authors of five studies were contacted for further information having read their titles and abstracts. Three replied however none of these studies fulfilled the inclusion criteria. Despite emailing the authors of

the other two studies on two different occasions we received no reply. Therefore, these studies were not included.

Assessment of risk of bias

Two reviewers (D.O.R. and R.G.) independently assessed the risk of bias for ITS using the EPOC (Effective Practice and Organisation of Care) risk of bias criteria and for RCTs using the Cochrane Collaboration's tool for assessing risk of bias (118, 119) . In any case of disagreement consensus was reached with a third reviewer (K.W.).

Results

A total of 2,193 studies were identified following removal of duplicates and five additional studies were located from hand searching references. A PRISMA flowchart (Figure 4.1) describes the flow of studies in the review. Fifty-eight full text studies were assessed for eligibility. At the end of the process five studies were eligible for inclusion in the systematic review. Of the five included studies, three were conducted in the United States, one in Europe and one in New Zealand (120-124).

The characteristics of the five included studies are summarised in Table 4.1.

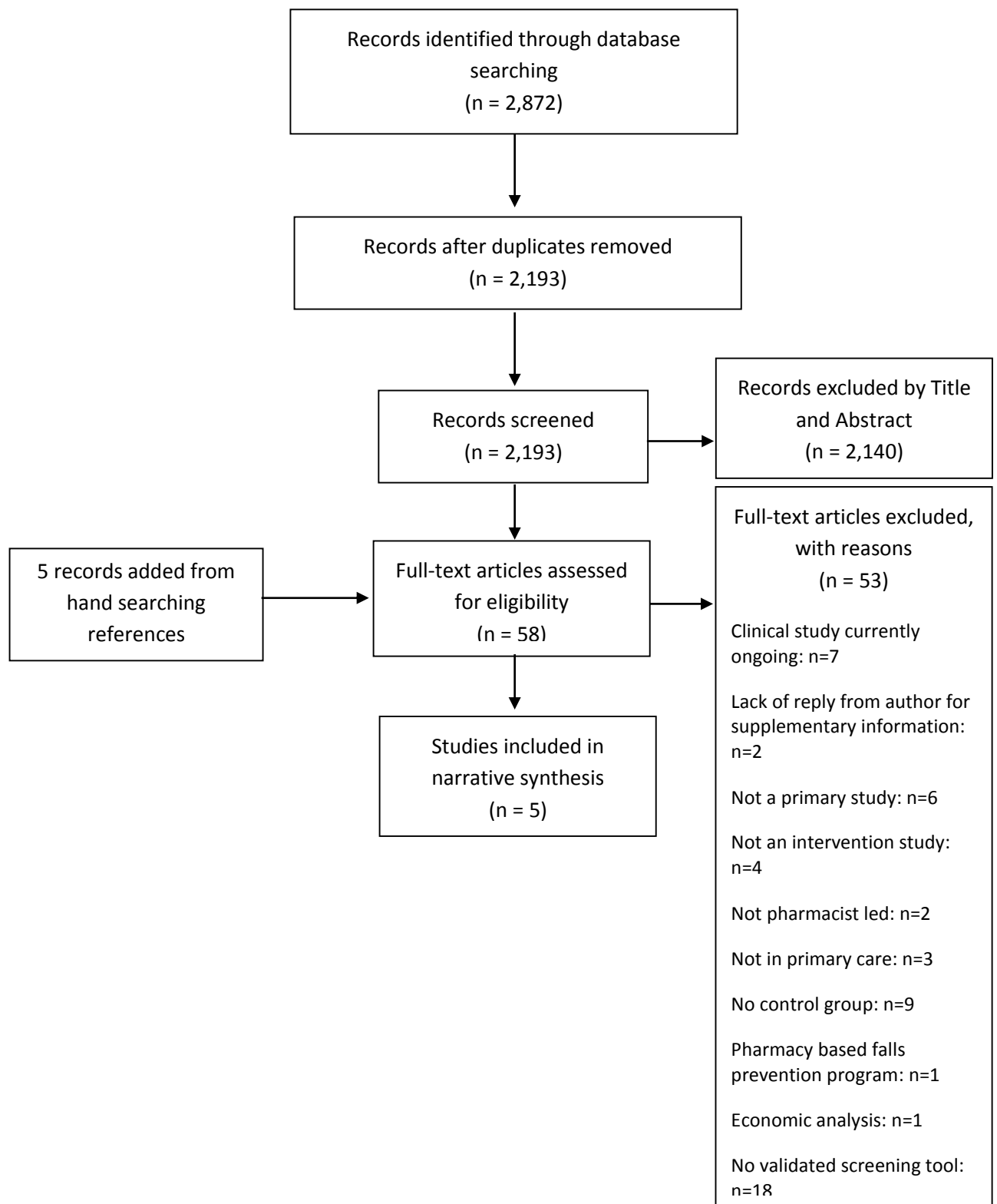


Figure 4.1 A PRISMA flowchart outlining the procurement of 5 included studies

Table 4.1 Study design, characteristics and outcomes of the included studies

Author and Year	Country	Setting	Study design	Aim of the study	No of patients	Mean age in years \pm S.D	% Female	Mean no of Rx meds per patient at baseline \pm S.D	Mean Summated MAI score per patient at baseline \pm S.D	Mean Summated MAI score per patient post intervention \pm S.D	Secondary outcomes
Bryant (2011)	New Zealand	General Practitioner (GP) practices in a primary health care	Randomised controlled trial (RCT)	The objective was to determine whether involvement of community pharmacists undertaking clinical medication reviews, working with general practitioners, improved medicine-related therapeutic outcomes for patients.	I: 269 C: 229	I: 75.9 (Range 64-92) C: 74.9 (Range 60-91)	I: 64.7% C: 52.4%	N/A	I: 5.1 C: 4.5	I: 3.1 C: 4.2	Change in the number of medicines used: More meds were started in the control group than the intervention group ($p<0.0001$). More dosage reductions and medicine switches in the intervention group than the control group ($p=0.037$). Recommendations implemented: 46% of recommendations were implemented, 16% partially implemented. Quality of life (SF-36): Improvement in emotional role (13.4 unit difference, $p=0.024$) and social functioning (7.7 unit difference, $p=0.019$)

											for the control group.
Hanlon (1996)	USA	A general medicine clinic of a Veterans Affairs Medical Center	Randomised controlled trial (RCT)	To evaluate the effect of sustained clinical pharmacist interventions involving elderly outpatients with polypharmacy and their primary physicians	I: 105 C: 103	I: 69.7 ±3.5 C: 69.9 ±4.1	I: 1.9 C: 0.0	I: 7.6 ± 2.8 C: 8.2 ± 2.7	I: 17.7± 6.2 C: 17.6± 6.1	I: 12.8± 7.2 C: 16.7± 7.1 (At 12 months)	Quality of life (SF-36): No significant difference between groups (p=0.99) Adverse Drug Event (ADE) (%): No significant difference between groups (p=0.19). Medication compliance (%): No significant difference between groups (p=0.88) Medication Knowledge (%): No significant difference between groups (p=0.29). VA prescribed meds: No significant difference between groups (p=0.83). General health care satisfaction: No significant difference between groups (p=0.70) Pharmacy related health care satisfaction: No significant difference between groups (p=0.52).

Raebel (2007)	USA	Kaiser Permanente Colorado (KPCO) Medical offices and pharmacies	Randomised controlled trial (RCT)	To determine whether a computerised tool that alerted pharmacists when patients ≥ 65 were newly prescribed potentially inappropriate medicines was effective in decreasing the proportion of patients dispensed these medications.	I: 29,840 C: 29,840	Median age (5 th , 95 th percentiles) I: 74 (66,88) C: 74 (66,88)	I: 57% C: 57%	Median (5 th , 95 th percentiles) I: 7 (1, 17) C: 7 (2, 16)	N/A	N/A	1.8% of intervention versus 2.2% of control had newly dispensed PIP (p=0.002). RRR = 16%, ARR = 0.3%. Dispensing rates differed between groups for amitriptyline (p<0.001; 37% RRR) and diazepam (p=0.02; 21% RRR).
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Richmond (2010)	England	All general practices in five Primary Care Trusts (PCTs)	Interrupted time series (ITS) and repeated measures studies	To estimate the effectiveness of pharmaceutical care for older people, shared between GPs and community pharmacists in the UK, relative to usual care. Usual care: Patients within each of the five primary care trusts (PCTs) on a waiting list before they received pharmaceutical care	551 were followed through pharmaceutical care	80.4 ± 4.1	43.2	8.1 ± 3.1	23.6 ± 19.5	N/A	Quality of life (SF-36): Mental score: No = 742, mean = 47.8, SD = 12.2 Physical score: No = 742, mean = 33.0, SD = 10.4. Nos of items on repeat prescription: No = 760, mean = 7.29, SD = 2.23 Serious adverse events: Pharmaceutical care model was not associated with any of the reported serious adverse events.
Taylor (2003)	USA	Three community-based family medicine clinics	Randomised controlled trial (RCT)	The program's primary purpose was to determine the effect of pharmaceutical care on the prevention, detection, and resolution of drug-related problems in high-	I: 33 C: 36	I: 64.4 ± 13.7 C: 66.7 ± 12.3	I: 63.6 C: 72.2	I: 6.3 ± 2.2 C: 5.7 ± 1.7	% of Inappropriate prescriptions according to each domain of the MAI at baseline for the intervention and control group.	% of Inappropriate prescriptions according to each domain of the MAI at 12 months for the intervention and control group.	Quality of life (SF-36); No significant difference between groups Hospitalizations and Emergency Department (ED) admissions: Fewer hospitalisations (2 v 11, p=0.003) and ED visits (4 v 6, p=0.044) in the

				risk patients in a rural community.						<p>The % of inappropriate prescriptions decreased in all 10 domains in the intervention group and increased in 5 domains in the control group.</p> <p>The domains in which prescribing was most frequently inappropriate were: dosage, correctness of directions, practicality of directions and expense.</p>	<p>intervention group compared to the control group.</p> <p>Compared to the control group, the intervention group were more likely to have controlled blood pressure (p=0.001), HBA1c (p=0.001), LDL cholesterol (p=0.001), INRs (p=0.048)</p> <p>Medication compliance: This score improved in the intervention group but not in the control group (p=0.115)</p> <p>Medication knowledge: This score improved in the intervention group but decreased in the control group (p=0.000)</p>
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ADE, Adverse drug event; ARR, Absolute risk reduction; C, Control; GP, General Practitioner; I, Intervention; INR, International normalised ratio; ITS, Interrupted times series; LDL, Low density lipoprotein; MAI, Medication Appropriateness Index; Meds, Medications; N/A, Not applicable; No, numbers; PCT, Primary Care Trust; RCT, Randomised Controlled Trial; RRR, Relative risk reductions; Rx, Prescription; SD, Standard Deviation; UK, United Kingdom; VA, Veterans Affairs.

Characteristics of included studies

Four of the studies involved a pharmacist carrying out a medication review and providing feedback to patients or their family physician (120-123). One study evaluated the effect of a computerised tool that alerted pharmacists at the point of dispensing when older patients were newly prescribed potentially inappropriate medications (124).

Bryant *et al.* involved pharmacists carrying out clinical medication reviews and providing feedback to the patient's physicians, while the control group received usual care which was not defined. Two hundred and sixty-nine patients were enrolled in the intervention group. The MAI score improved more in the intervention group than in the control group (mean change in MAI score -2.0 in the intervention group; -0.3 in the control group, $p < 0.001$). There were more medicines started in the control group than the intervention group ($p < 0.0001$), while there were more dosage reductions and medicine switches in the intervention group than in the control group ($p = 0.037$) (120).

Hanlon *et al.* evaluated the effect of a pharmacist-led review of patient's medical charts, followed by a clinical recommendation to the family physician in 105 cases. The researchers also provided compliance strategies to the patients. Patients in the control group had their medications reviewed by a clinical nurse, however the clinical pharmacist had no interaction with the patients or their clinicians during the study period. The MAI score improved more in the intervention group than in the control group (mean change in MAI score -4.9 in the intervention group; -0.9 in the control group, $p < 0.001$). There was no significant difference between groups regarding

adverse drug events (ADEs), $p=0.19$ or veterans affairs (VA) medicines prescribed $p=0.83$ (121).

Taylor *et al.* examined the effect of a pharmacist intervention that provided medication education to patients and therapeutic recommendations to their family physicians following a medication review in 33 older adults. A pharmacist evaluated the pharmacotherapy of each patient in the control group however no recommendations were reported to the patient or their physician. The percentage of inappropriate prescriptions decreased in all 10 MAI domains in the intervention group and increased in five domains in the control group. Clinical outcomes such as hypertension, diabetes mellitus, dyslipidaemia, anticoagulation, hospitalisations and emergency department (ED) admissions were reported. Compared to the control group, the intervention group were more likely to have controlled blood pressure ($p=0.001$), HBA1_c ($p=0.001$), low density lipoprotein (LDL) cholesterol ($p=0.001$) and international normalised ratio (INRs) ($p=0.048$). There were fewer hospitalisations (2 vs 11, $p=0.003$) and ED visits (4 vs 6, $p=0.044$) in the intervention group compared to the control group (122).

Richmond *et al.* developed pharmaceutical care plans among pharmacists and family physicians. The pharmaceutical care model involved pharmacists carrying out medication reviews and collaborating with physicians, patients and carers to identify issues with compliance and adverse drug reactions. It was hypothesised that the review process would also serve to encourage the prescribing of generic medicines and reduce health costs. Following this, pharmacists conducted monthly medication reviews with feedback to the physicians. The usual care group consisted of patients

within each of the five primary care trusts (PCTs) on a waiting list to receive pharmaceutical care. A total of 551 participants completed the study. Results demonstrated that the pharmaceutical care model did not affect the appropriateness of prescribing (mean change in UK-MAI score from baseline to the end of the intervention was -0.26, $p>0.05$). Also, the pharmaceutical care model was not associated with any of the reported serious adverse events (123).

Finally, Raebel *et al.* estimated the effect of a computerized tool that alerted pharmacists at the point of dispensing when older patients were newly prescribed potentially inappropriate medicines (PIMs). Pharmacists and physicians collaborated to develop a targeted medication list for the intervention group based on the Beers, Zhan and Kaiser Permanente Care Management Institute lists of medications to be avoided in older people (125-127). The intervention group consisted of 29,840 patients. When a patient randomised to the intervention group was prescribed a new potentially inappropriate medication, the pharmacist was notified via a medication alert generated from an electronic database. Pharmacists were required to complete a note on a standard intervention template before printing a label to dispense the prescription. Pharmacists were then instructed to telephone the prescribing physician to suggest alternatives. Patients in the control group received medication prescribing and dispensing according to usual clinical practice. When medications were dispensed, monitoring and patient management proceeded according to the prescriber's usual procedures. Over the course of the study, 1.8% of intervention group patients versus 2.2% of control group patients had a newly prescribed PIM ($p=0.002$). The relative risk reduction (RRR) and absolute risk reduction (ARR) were

16% and 0.3% respectively. The dispensing rates for amitriptyline ($p < 0.001$, RRR 37%) and diazepam ($p = 0.02$, RRR 21%) also differed significantly between groups (124).

The appropriateness of sample sizes was addressed by Hanlon *et al.* and Richmond *et al.* (121, 123). Taylor *et al.* and Raebel *et al.* did not carry out a sample size calculation (122, 124). Finally Bryant *et al.* calculated the sample size based on the quality of life tool, the SF-36, however it is unclear how many physicians were enrolled in each arm of the study (120).

Characteristics of the pharmacist's interventions

The characteristics of the criteria applied, healthcare professionals involved in each study and details of the pharmacist interventions are summarised in Table 4.2. The MAI criteria were used in four of the studies (109, 120-123). In the Raebel *et al.* study the Beers criteria and Zhan criteria were used (124-127). According to Richmond *et al.* and Raebel *et al.*, pharmacists did not have access to medical notes (123, 124). A medication review was conducted in four studies (120-123). Two studies, Hanlon *et al.* and Taylor *et al.* involved pharmacists providing patients with written educational materials as part of the intervention (121, 122). Pharmacists in four of the studies provided feedback to the physicians orally or in the written format (120-122, 124). Two of the studies provided feedback via both methods of communication (121, 122). It is not clear from the Richmond *et al.* study how feedback was communicated to physicians. Finally one study involved an educational meeting with physicians (123).

Table 4.2 Characteristics of the pharmacist's interventions

Author, year, country	Criteria applied	List of healthcare professionals involved	Number of healthcare professionals involved	Access to lab data	Access to medical notes	Medication review carried out	Patient counselling undertaken	Patients given educational material	Written communication with physicians	Oral communication with physicians	Educational meeting with physicians
Bryant (2011), New Zealand	MAI	Pharmacists, Physicians	Two	No	Yes	Yes	Yes	No	Unclear	Yes	No
Hanlon (1996), USA	MAI	Pharmacists, Physicians, Nurses	Three	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Raebel (2007), USA	Beers, Zhan, ^a KPCMI	Pharmacists, Physicians	Two	No	No	No	No	No	No	Yes	No
Richmond (2010), England	MAI	Pharmacists, Physicians	Two	No	No	Yes	Unclear	No	Unclear	Unclear	Yes
Taylor, (2003), USA	MAI	Pharmacists, Physicians, Nurses	Three	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes

^a KPCMI: Kaiser Permanente Care Management Institute.

Results of the risk of bias assessment

The results of the risk of bias are presented in Tables 4.3 and 4.4. Common sources of bias included inadequate sample size, performance bias and spectrum bias. Overall, the authors considered four of the five studies to be at high risk of bias.

Synthesis method

Due to the heterogeneity of the interventions and outcome measures reported a narrative synthesis was carried out.

Table 4.3 Methodological quality of RCT studies included in the review as carried out by the Cochrane Collaboration's tool (118)

Authors	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias	Risk of bias
	Random sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other source of bias	Overall risk of bias
Bryant 2011	High risk	High risk	Unclear	Low risk	High risk	Low risk	Unclear	High
Hanlon 1996	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	High risk	High
Raebel 2007	Low risk	Unclear	Low risk	Unclear	Low risk	Low risk	Unclear	Unclear
Taylor 2003	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	High risk	High

Table 4.4 Methodological quality of ITS study included in the review as carried out by the EPOC checklist (119)

Author	Was the intervention independent of other changes?	Was the shape of the intervention effect pre-specified?	Was the intervention unlikely to affect data collection?	Was knowledge of the allocated interventions adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Was the study free from selective outcome reporting?	Was the study free from other risks of bias?	Overall risk of bias
Richmond 2010	Low risk	Low risk	High risk	Low risk	Unclear risk	High risk	High risk	High

Discussion

Statement of principal findings

This systematic review examined the impact of pharmacist-led interventions on appropriateness of prescribing in older adults in primary care. Interventions across the five studies consisted of structured medication reviews or computer alerts. Three of the five studies reported an improvement in the MAI score in the intervention group compared to the control group (120-122). Raebel *et al.* reported a reduction in newly dispensed PIMs (124). Richmond *et al.* reported that pharmaceutical care undertaken by community pharmacists did not significantly change the appropriateness of prescribing in older patients. One of the limitations from this study was that pharmacists were unable to gather detailed clinical records for patients. This may have led to an underestimation of the true MAI score (123). In three of the studies pharmacists had access to the patients' medical notes (120-122). This may have impacted on the nature and scope of the medication review by pharmacists. Another limitation was that pharmacists reported difficulties in accessing patients and physicians in order to prepare and discuss the pharmaceutical care plan. This was despite the fact that joint collaborative training on pharmaceutical care was provided to pharmacists and physicians (123). The two studies that involved pharmacists providing patients with written education materials may have further improved their understanding of and compliance with medicines (121, 122). In the study by Bryant *et al.* the medication review was conducted in the pharmacy or at the patient's home. Although the MAI score improved more in the intervention group than in the control group approximately

40% of the pharmacist recommendations were not implemented by the physicians. It is not known whether the non-implementation was due to the physician-pharmacist relationship or whether there were other barriers involved (120). According to Raebel *et al.*, the absolute difference in dispensing numbers between intervention and control groups was minimal. This was despite the fact that pharmacists and physicians collaborated to develop a list of medicines for the intervention, specific intervention guidelines and patient counselling scripts. The study highlights the difficulty in modifying prescribing behaviour even though the intervention was fully advocated by the physicians (124). Finally, in the study by Hanlon *et al.* the target population was elderly male veterans. This may impact on the generalisability of the study findings (121).

Clinical significance of MAI change

In the studies carried out by Hanlon *et al.* and Taylor *et al.* the authors conclude that the clinical significance of the change in MAI remains unclear and highlight this as a potential limitation (121, 122). Bryant *et al.* suggest further research be carried out to determine the relationship between the MAI and hospitalisations rates (120). Finally in the Richmond *et al.* study the pharmaceutical care model carried out by pharmacists did not significantly change the appropriateness of prescribing or quality of life in older people (123).

A narrative review identified seven studies that evaluated the predictive validity of the MAI in relation to various health outcomes (109). Three studies involved Veterans Affairs (VA) outpatients or VA medical centres across the USA (128-130). In these studies, higher MAI scores were significantly associated with unscheduled

ambulatory or emergency department (ED) visits and inadequate blood pressure control, adverse drug events using modified MAI scores and adverse drug reactions by drug-disease interaction criteria (128-130).

Results in the context of the current literature

A systematic review by Kaur *et al.* evaluated various interventions and strategies to reduce inappropriate prescribing in older people in primary and secondary care settings. The review highlighted that pharmacist interventions were successful in reducing inappropriate prescribing. Other interventions that demonstrated positive effects on prescribing included, computerised support systems, geriatrician's services and multidisciplinary team work. However, there were mixed responses for educational interventions aimed at improving inappropriate prescribing due to the variability in assessment methodologies. The effect of regulatory policies as an intervention was also variable (131). A further narrative review appraised prospective and intervention studies that focused on the use of potentially inappropriate medicines (PIM's) in community-dwelling older adults. Intervention studies that were included aimed to change the prescribing patterns of physicians. The majority of included studies focused on the prevalence of PIM's. Several others analysed the relationship between PIM's and falls, cognitive function, sleep and quality of life. This narrative review recommends more collaborative multidisciplinary team approaches that include pharmacists to reduce the use of PIM's. It also suggests that mixed-methods research could enhance the quality of interventions to address PIM use (117). A Cochrane review examined 12 intervention

studies including pharmacist-led studies aimed at improving appropriate polypharmacy for older people across healthcare settings (112). In hospital settings, pharmacists provided pharmaceutical care in outpatient clinics and inpatient departments. In primary care, pharmacist interventions included medication reviews with feedback to physicians and medicine education to patients. Finally, in nursing homes, pharmacists worked with other healthcare professionals on case conferences and provided education to staff members. A drug management service was also provided. The post-intervention results demonstrated a mean difference of -3.88 (95% CI -5.40 to -2.35) in the change in MAI score in favour of the intervention group compared with the control group across the five studies. This updated review published in 2014 was based on a previous Cochrane review carried out by the same authors. It included two additional studies from the previous review (112) .

A review by Castelino *et al.* evaluated 12 interventions involving pharmacists that focused on reducing inappropriate prescribing in older adults across different healthcare settings. The selected studies highlighted pharmacists working independently or as part of multidisciplinary healthcare teams. The services provided by pharmacists commonly involved some form of medication review, highlighting the important role that pharmacists play in optimising medication use for this group of patients (113).

The current systematic review has highlighted that pharmacist-led interventions involving access to medical notes and medication reviews conducted in physician practices with feedback to physicians may improve prescribing appropriateness in community-dwelling older adults. The findings are broadly in-keeping with other

reviews including a recent systematic review with meta-analysis conducted to determine the effectiveness of pharmacist interventions to reduce PIP in older adults admitted to hospital. The review concluded that pharmacists carrying out medication reviews as part of multidisciplinary patient care teams may improve the quality of prescribing in older hospitalised patients (112, 115, 117, 131).

In addition, the findings are consistent with the evidence highlighted that the quality of prescribing for older people in primary care could benefit from pharmacist-physician collaboration.

Clinical implications and areas for further research

This review has implications for clinical practice and future research, in particular with respect to the emerging role that pharmacists play in moderating medication appropriateness in primary care.

There is a growing need for improved collaboration between physicians and pharmacists in order to optimise prescribing practices in primary care. Collaborative multidisciplinary models can improve the care of older adults with chronic multimorbidities (132). The PINCER trial is an example of such a model. It highlighted the benefit of a pharmacist-led intervention in general practices in the UK. The practices were cluster randomised to a pharmacist-led information technology intervention group or a control group. This trial demonstrated that the PINCER intervention was effective at reducing medication errors in general practice (133). Schmader *et al.* demonstrated that compared with usual care, inpatient and outpatient geriatric evaluation and management programs involving pharmacists

reduced suboptimal prescribing in frail elderly patients. The outpatient geriatric teams also reduced serious adverse drug reactions (110).

The diverse range of outcome measures used in studies of prescribing appropriateness has made it difficult to make firm conclusions in this field. Ideally, prescribing outcome measures should be linked to important clinical outcomes such as morbidity or mortality. A pan-European study is currently underway and may add clarity to this issue: The OPERAM study (Optimising thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly) aims to reduce the rates of over and under prescribing of medications among multimorbid older European adults. While PIP is one measure among others at measuring optimal prescribing there is an underreporting of medication errors in the literature. One major component of this large multi-centre randomised clinical trial will be the use of a sophisticated software tool to optimise medication therapy and to determine whether the applied intervention can improve clinical outcomes such as drug related admissions (DRAs), humanistic outcomes such as quality of life and reduce healthcare costs (<https://operam2020.tp21.com>).

Educational outreach interventions or “Academic detailing” provided by pharmacists (or other clinicians) to physicians in primary care is an area for further research. The term “Academic detailing” was coined by Jerry Avorn MD over thirty years ago (134). Clinical educators, who are usually pharmacists, nurses or physicians are trained to provide accurate, balanced, non-commercial and up to date synthesis of the best clinical evidence in an engaging format with healthcare physicians (134). Information highlighted to physicians often includes recommendations about alternative

treatment regimens or non-pharmacological interventions where appropriate. These recommendations are designed to complement the clinical judgement of a physician and not to replace it (135). This evidence-based strategy has been shown to be an effective means of changing physician behaviour and improving patient care (136). For example, a pharmacist-led intervention comprising academic detailing demonstrated an improvement in statin prescribing in high-risk patients in primary care (137).

There is a dearth of research examining the cost-benefit analysis of pharmacist-led interventions to improve prescribing patterns in healthcare. Cowper *et al.* conducted a cost analysis of a previously reported randomised control trial (121, 138). The total cost of the clinical pharmacist intervention was \$120 per patient per year. This intervention was a cost-effective means at improving prescribing among elderly outpatients (138). In the PINCER trial, the cost per error avoided was estimated by incremental cost-effectiveness analysis. The pharmacist-led intervention had a 95% probability of being cost effective at various time points throughout the trial (133). The economic benefits of using validated screening tools in primary care are currently limited and require further research.

Strengths and weaknesses

This is the first systematic review to focus specifically on the impact of pharmacist-led interventions on prescribing appropriateness in older adults in primary care. An explicit and robust methodology was applied to identify and synthesise the study findings. However, the findings of the review need to be interpreted in the context of the study limitations. Firstly, the methodological quality of the studies was poor overall, limiting the generalisability of the findings. Secondly, despite applying a comprehensive search strategy, only five studies were eligible for inclusion in the review. Thirdly, if the following terms i.e. inappropriate prescribing, potentially inappropriate prescribing, suboptimal prescribing were applied across all databases it may have narrowed down the searches. Subsequently, the lack of standardised reporting across studies limited the statistical pooling of data. Moreover, three studies reported an improvement in the MAI score for the intervention group compared to the control group, however the effect sizes are small which highlights the need for further research to assess the impact of pharmacist-led interventions in primary care. Furthermore, the clinical impact of reducing surrogate markers such as the MAI remains unknown and requires further investigation. However, one of the aims of the OPERAM study is to link prescribing outcome measures with clinical outcomes such as hospital admissions. Finally, large cluster-randomised control trials that are methodologically robust and have a long duration of follow up are needed to address patient focused outcomes. In addition, reviews on the appropriateness of prescribing are warranted among other vulnerable populations including paediatric patients, drug users, homeless people and prisoners.

Conclusion

This review concludes that pharmacist-led interventions involving access to medical notes and medication reviews conducted in physician practices with feedback to physicians may improve prescribing appropriateness in community-dwelling older adults. Interventions where computer alerts help to inform pharmacists of potentially inappropriate medicines may also improve prescribing appropriateness. However, it is unclear if these interventions result in clinically significant improvements in patient outcomes. Further high-quality research should be conducted to explore the generalisability of these interventions. Finally, the role of a pharmacist working as part of a multidisciplinary primary care team requires further investigation to optimise prescribing in this group of patients.

Chapter 5. GPs' perspectives on prescribing for older people in primary care: a qualitative study

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Abstract

Aims

The aim of this study was firstly to reveal the determinants of GP prescribing behaviour for older adults in primary care and secondly to elicit GPs' views on the potential role for broad intervention strategies involving pharmacists and/or information technology systems in general practice.

Methods

Semi-structured qualitative interviews were carried out with a purposive sample of GPs. Three multidisciplinary researchers independently coded the interview data using a framework approach. Emerging themes were mapped to the Theoretical Domains Framework (TDF), a tool used to apply behaviour change theories.

Results

Sixteen GPs participated in the study. The following domains in the TDF were identified as being important determinants of GP prescribing behaviour: "Knowledge", "Skills" "Reinforcement", "Memory Attention and Decision Process", "Environmental Context and Resources", "Social influences", "Social/Professional Role and Identity". Participants reported that the challenges associated with prescribing for an increasingly older population will require them to become more knowledgeable in pharmacology and drug interactions and they called for extra training in these topics. GPs viewed strategies such as academic detailing sessions delivered by pharmacists or information technology systems as having a positive role to play in optimising prescribing.

Conclusion

This study highlights the complexities of behavioural determinants of prescribing for older people in primary care and the need for additional supports to optimise prescribing for this growing cohort of patients. Interventions that incorporate, but are not limited to interprofessional collaboration with pharmacists and information technology systems, were identified by GPs as being potentially useful for improving prescribing behaviour, therefore require further exploration.

What is known about this subject?

- Providing optimal medication management for older people is a challenge for GPs.
- Prescribing for older people can result in medication-related problems and preventable drug-related morbidity.
- As the main prescribers of medication in primary care, GPs can provide a deeper insight into the complexities of prescribing for these patients.

What this study adds

- Prescribing for the growing older population is viewed by GPs as a significant challenge in their clinical practice.
- GPs are calling for additional support in order to help them manage and treat these patients.
- Academic detailing, an approach that provides GPs with accurate, non-biased and evidence-based information, is viewed by GPs as a potentially useful way to help optimise their prescribing. Information technology systems are also identified by GPs as having a role to play in supporting safer prescribing.

Introduction

Providing optimal care for older adults creates many challenges for healthcare providers especially general practitioners (GPs) (11-13, 15). Appropriate prescribing of medications is a significant challenge as older adults can present with multiple conditions for which multiple medications are often indicated (1, 6). Age related changes in pharmacokinetics and pharmacodynamics contribute to the challenge of appropriate prescribing (139). Inappropriate prescribing results in preventable drug-related morbidity (PDRM) including adverse drug events (ADEs), hospital admissions and mortality (107, 140, 141). Potential PDRM events occur in 1.0% of patients attending general practice, with the most common PDRM events relating to the use of non-steroidal anti-inflammatory (NSAID) medicines in patients with congestive heart failure or hypertension, lack of monitoring in patients prescribed angiotensin converting enzyme (ACE) inhibitors and the use of hypnotic-anxiolytic agents (142).

As GPs are the main prescribers of medication in primary care, understanding the factors influencing GP behaviour in relation to prescribing is a first step in reducing PDRM and improving clinical outcomes (143). Previous research has shown that factors influencing GP prescribing decisions include medication effectiveness, associated risks, medication costs and patient characteristics or preferences (144). Other influences include factors which relate specifically to the individual GP such as post-graduate qualifications or training (145), the prescribing behaviour of hospital consultants (146), or advertising by the pharmaceutical industry (147). However, how best to intervene on these influences to improve GP prescribing is not known. It has been proposed that knowledge of the key determinants of health care professionals'

(HCP) behaviour can be used to theoretically inform interventions that aim to change that behaviour (148). Additionally, qualitative research with HCPs can inform and optimise the delivery of subsequent interventions.

The Theoretical Domains Framework (TDF) is an overarching framework of theories that identifies the specific process underlying successful behaviour change (149). It consists of 14 domains and 84 component constructs (150). The TDF has been used to identify key theoretical domains that are perceived to influence HCPs behaviours (150). For example, Cullinan *et al.* used the TDF to identify key influences of potentially inappropriate prescribing (PIP) by hospital doctors such as insufficient training in prescribing for older people (151).

The aim of this study was firstly to reveal the determinants of GP prescribing behaviour for older adults in primary care and secondly to elicit GPs' views on the potential role for broad intervention strategies that is, involving pharmacists and/or information technology systems in general practice. Participants were also encouraged to suggest any other types of intervention that they thought would be feasible and useful.

Methods

Design

Semi-structured qualitative interviews were conducted with GPs in primary care to explore their experiences of prescribing for patients aged 65 and older and their views on the potential role for interventions involving pharmacists and/or information technology systems in general practice. This interview method was

chosen due to its flexible and interactive nature and its ability to achieve comprehensive coverage of the topic discussed (152). The descriptions of their experiences were analysed using qualitative methods and mapped to the TDF framework to reveal behavioural determinants.

Sampling

This study was conducted in County Cork, Ireland. A purposive sample of GPs in teaching practices associated with University College Cork (UCC) were initially invited to participate. The purposive sampling strategy was based on years of experience (≥ 10 or ≤ 10 years), practice location (% urban population of GP practice location) and practice size (single or group practice). There were no inclusion or exclusion criteria for participants other than a requirement to be in active clinical practice. D.O.R. contacted potential participants by telephone and a brief summary of the study was given. In some cases, snowball sampling was used when participants who were based in single rural practices and had already been interviewed were asked to identify other GPs who they thought might be interested in participating. The nominated GPs were then sampled according to the needs of the sampling frame.

Two pilot interviews were conducted. Following review of the data and topic guides, the authors agreed to include the data generated from the pilot interviews as it was highly relevant to the study question.

The method developed by Francis *et al.* was used to determine data saturation (153). Firstly, the authors agreed *a priori* that the first 10 participants (initial analysis sample) represented adequate diversity on the pre-specified stratification factors

(years of experience, gender, practice location and practice size). Secondly, it was agreed *a priori* that after 10 interviews were conducted data saturation was reached once three consecutive interviews did not contribute further to thematic development (stopping criterion). The stopping criterion was tested after each successive interview e.g. 11, 12, 13. At interview 13, a further 3 interviews were carried out to identify new themes. However, these additional interviews did not contribute to the further development of emerging themes. Therefore, interview 16 was defined as the point of data saturation.

Data collection

The interviews were carried out by one researcher (D.O.R.) at the GPs surgeries between March 2015 and August 2015.

A topic guide was developed based on previous literature and was agreed on by all authors (154, 155). It was iteratively refined after each interview was transcribed and analysed to pursue emerging themes. Further refinements were reviewed by another author (CS) and examples are provided as supplementary material to show its continuous development as the interviews proceeded (See Appendix III). Demographic details were collected including practice location, GP gender, years' experience as a GP and number of GPs, including GP registrars where relevant, working in the practice. In addition to questions on their experience of prescribing for older patients, participants were asked for their views on the potential role for interventions (i.e. involving pharmacists and/or information technology systems) in general practice.

The interviews were audio-recorded, fully transcribed and saved in QSR International's NVivo Qualitative Data Analysis Software (V.10.22) to facilitate analysis (76). Field notes were written and used to facilitate preliminary familiarisation with emerging themes immediately after each interview.

Analysis

The framework approach, which consists of five stages, was used to analyse the data (152). The first phase involved reading and re-reading each transcript as well as listening to interview recordings to become familiar with the content. The second phase involved identifying a thematic framework. Due to the specifics of the research aim, a deductive approach was taken with agreement by the authors to use the Theoretical Domains Framework (TDF) *a priori*. The next phase was indexing: this involved open coding (carried out by D.O.R.) and development of a coding scheme. The fourth phase involved arranging data into domains of the TDF and generating charts. In some cases, the data was relevant to more than one domain and this resulted in "double coding" of the data. The last phase involved interpreting the data by finding associations between themes with the aim of providing explanations for them. To enhance the credibility of coding, three multidisciplinary researchers (D.O.R., C.S., and S.B.) independently coded a sample of the transcripts.

The consolidated criteria for reporting qualitative research (COREQ) statement was used to guide reporting of the findings (see Appendix III) (156).

Ethical approval for this study was granted by the Clinical Research Ethics Committee of the Cork University Teaching Hospitals (reference ECM 3 (mmm) 14/04/15 & 4 (k) 07/10/14) (See Appendix IX). All participants provided written informed consent.

Results

Sixteen interviews were conducted in total. The interviews ranged from 9 minutes to 31 minutes (mean interview length 19 minutes). The mean duration of participating GPs' medical experience was 17 years. The number of GPs working in a practice ranged from 1 to 6. The characteristics of participants interviewed are provided in Table 5.1.

The definition of all 14 TDF domains as described by Cane *et al.* together with supporting quotes from participants are shown in Table 5.2 (150).

Almost all of the TDF domains were seen to be relevant to the study data but the domains presented in detail here were prioritised because of the emphasis placed on them by participants, the frequency of occurrence of the domain across all the transcripts, and the consensus agreement of the authors.

Table 5.1 Characteristics of GP participants

General Practitioner (GP)	Gender	Years of medical experience	% Urban population of GP practice location	No. of GPs in the practice	No. of GP registrars in the practice
1	F	4	19.5	2	0
2	F	20	25.7	4	1
3	M	33	25.7	4	1
4	F	20	25.7	1	0
5	F	4	100	2	0
6	M	25	25.7	4	1
7	F	4	8.4	2	0
8	M	20	100	2	0
9	M	35	25.7	4	1
10	F	19	25.7	1	0
11	F	13	100	3	1
12	F	4	25.7	4	1
13	M	3	19.5	2	0
14	M	30	100	3	1
15	M	14	8.8	6	0
16	M	27	25.7	4	1

Table 5.2 TDF domains, explanatory constructs and supporting quotes (150)

Domain (definition) & Constructs	Domain reported in the study results	Supporting quotes
1. Knowledge (An awareness of the existence of something) Constructs <ul style="list-style-type: none"> • Knowledge (including knowledge of condition/scientific rationale) • Procedural knowledge • Knowledge of task environment 	✓	<p><i>“... It’s going to have a huge impact on general practice and GPs, I think we’ll need to try and continue to improve our skills in that area and I think care of the elderly... will be a speciality ... it’s going to present a lot of challenges in terms of knowing the pharmacology and interactions.” (GP11)</i></p> <p><i>“Three times a week for 5 minutes I meet a drug rep ... so while we take it with a pinch of salt, because we know it’s biased we inevitably are influenced by drug reps” (GP15)</i></p>
2. Skills (An ability or proficiency acquired through practice) Constructs <ul style="list-style-type: none"> • Skills/Skills development • Competence • Ability • Interpersonal skills • Practice • Skill assessment 	✓	<p><i>“I personally think that we should have to every 6 or 12 months sit some kind of exam in prescribing ...because prescribing is so desperately important and I think the only way I would actually change the way I practice is if there was some kind of revalidation.....” (GP15)</i></p> <p><i>“We find that in General Practice there are so many important areas we need to up skill in ... And this is a particularly important one (Educational training), and I think you’d probably find that most GPs would agree with that.” (GP5)</i></p>
3. Social/Professional Role and Identity (A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting) Constructs <ul style="list-style-type: none"> • Professional identity/ Social identity • Professional role • Identity/ Group identity • Professional boundaries • Professional confidence 	✓	<p><i>“I think some of the hospital sector, don’t fully understand the nature of general practice ...I saw a person with a renal problem and I was in their house I rang the Urology (team) because they had a nephrostomy tube and they were asking me what his creatinine was..... they just had no idea that you don’t have a portable creatinine monitor by your side....” (GP8)</i></p> <p><i>“As a GP, you have a role as a co-ordinator of care, and you’d have the most up to date record of everything that’s going on.” (GP5)</i></p>

<ul style="list-style-type: none"> • Leadership • Organisational commitment 		
<p>4. Beliefs about Capabilities (Acceptance of the truth, reality, or validity about an ability, talent or facility that a person can put to constructive use)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Self-confidence • Perceived competence • Self-efficacy • Perceived behavioural control • Beliefs • Self-esteem • Empowerment • Professional confidence 	X	<p><i>“I am slow to start new medications for 6 to 12 months I leave it out on the market and I think sometimes other professionals ... may not think of that in a positive way but that’s the way I am.” (GP16)</i></p> <p><i>“Sometimes there’s this feeling going around unless you are using the new medications you are sometimes behind the times or a bit old fashioned ... but sometimes it might be that there’s much better evidence for the older medication or you know it’s been studied a lot more and there might be very little evidence for the new one and the new one might be 5-6 times the cost if not more.” (GP8)</i></p>
<p>5. Optimism (The confidence that things will happen for the best or that desired goals will be attained)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Optimism • Pessimism • Unrealistic optimism • Identity 	X	<p><i>“We need enhanced roles of the ... pharmacists, the practice nurses, advanced nurse practitioners, more community nurse workers as well as public health nurses you know such as dementia care nurses and things like that. I think all those things will sort of help give a better standard. I think it will happen bit by bit.” (GP8)</i></p> <p><i>“There needs to be a common goal that the patient is a priority and it is very significantly absent from management and health services. Ok, they do not look at the patient goal because the managers regard the management as being totally isolated from health responsibility. With any luck, we’ll bring that around.” (GP3)</i></p>
<p>6. Beliefs about Consequences (Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Beliefs • Outcome expectancies 	X	<p><i>“One issue that springs to mind is... benzodiazepine prescribing, so you would have a cohort of elderly patients who have been prescribed benzodiazepines for a very long period of time, that you wouldn’t be in a position to be really thinking about stopping them, but certainly you would wonder if, certain events such as a fall, an episode of confusion, could be related to these particular medications.” (GP5)</i></p>

<ul style="list-style-type: none"> • Characteristics of outcome expectancies • Anticipated regret • Consequents 		<p><i>“One of the biggest problems at the moment is the generic substitution, it is confusing the hell out of all the elderly patients and that they are getting different pills, different capsules instead of pills and shapes and colours and sizes and names are all changing.” (GP3)</i></p>
<p>7. Reinforcement (Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Rewards (proximal/distal, valued/not valued, probable/improbable) • Incentives • Punishment • Consequents • Reinforcement • Contingencies • Sanctions 	✓	<p><i>“I’m pretty sure it’s out there somewhere that it’s the biggest source of litigation I think for GPs is prescribing or prescribing errors.” (GP13)</i></p> <p><i>“The other thing I suppose is whether this (educational training) will qualify for external CPD points. Because we’re all required to get 20 external points and internal points ..., and certainly if it could be something that was worth internal and external points, I think it could be beneficial.” (GP5)</i></p>
<p>8. Intentions (A conscious decision to perform a behaviour or a resolve to act in a certain way)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Stability of intentions • Stages of change model • Transtheoretical model and stages of change 	X	<p><i>“Sometimes it’s nearly easier to wait until the outpatient’s letter come and then start the medication.” (GP7)</i></p> <p><i>“But if it was something like methotrexate...even thinking about it now would give you the heebee jeebees ... you’ve somebody elderly in front of you and your really not sure, I just don’t think you can prescribe it really you know.” (GP11)</i></p>
<p>9. Goals (Mental representations of outcomes or end states that an individual wants to achieve)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Goals (distal/proximal) • Goal priority • Goal/target setting 	X	<p><i>“I think we are all in it for the side of the patient like what you want is a patient who’s prescribed appropriate drugs, at an appropriate dose for appropriate lengths of time.” (GP10)</i></p>

<ul style="list-style-type: none"> Goals (autonomous/controlled) Action planning Implementation intention 		<p><i>“There are areas where I believe ...for a pharmacist within the clinical environment. And I think that would work and certainly is one area we would love to trial and have tried to do before. It works in various areas in the UK. It’s been very successful.” (GP3)</i></p>
<p>10. Memory, Attention and Decision Processes (The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives)</p> <p>Constructs</p> <ul style="list-style-type: none"> Memory Attention Attention control Decision making Cognitive overload/tiredness 	✓	<p><i>“But if it was something like methotrexate even thinking about it now would give you the heebie jeebies... you’ve somebody elderly in front of you and you’re really not sure, I just don’t think you can prescribe it really you know.” (GP11)</i></p> <p><i>“... if you do need to use something ... bearing in mind their cardiovascular risk, bearing in mind their falls risk that go with lots of the sedative medication, antipsychotics, sleeping tablets ... I think that’s my biggest bugbear, difficulty.” (GP13)</i></p>
<p>11. Environmental Context and Resources (Any circumstance of a person’s situation or environment that discourages or encourages the development of skills and abilities, independence, social competence and adaptive behaviour)</p> <p>Constructs</p> <ul style="list-style-type: none"> Environmental stressors Resources/material resources Organisational culture/climate Salient events/critical incidents Person x environment interaction Barriers and facilitators 	✓	<p><i>“If you’re really busy sometimes and I’m just being honest, you just print off their last month’s prescription and you’ll keep going with that, you know.” (GP4)</i></p> <p><i>“We’re very lucky that we have a very good relationship with the local pharmacist here they are very, very good and so we would be on to them a number of times a day ... particularly for people who come out from hospital whereas sometimes it isn’t clear what dose of medications they’re on.” (GP8)</i></p>
<p>12. Social influences (Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours)</p> <p>Constructs</p> <ul style="list-style-type: none"> Social pressure/Social norms/ Social comparisons Group conformity/Group norms/Group identity 	✓	<p><i>“... so people do present saying I saw the ad on the telly (for an anticholinergic medication for urinary incontinence) and I have the overactive bladder and you’re thinking anticholinergics and you’re 75 but they still expect it you know.” (GP1)</i></p>

<ul style="list-style-type: none"> • Social support • Power • Intergroup conflict • Alienation • Modelling 		<p><i>“Any of those on the benzos you’d be trying to pull them all off it... Very hard, very hard. ...And in spite of you talking about the risk of falls and obviously slowly weaning off ...but very hard to get patients off these tablets that are not essential really you know.” (GP7)</i></p>
<p>13. Emotion (A complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Fear • Anxiety • Affect • Stress • Depression • Positive/negative affect • Burn-out 	X	<p><i>“I’m worried, I’m always worried about renal function, I’m worried about anti-inflammatories and hypertension, I’m worried about risk of bleeding, I’m worried about side-effects, probably I should worry more about drug interaction and I don’t.” (GP15)</i></p> <p><i>“But as regards other people highlighting it (prescribing errors) I don’t mind, I’m just embarrassed really.” (GP11)</i></p>
<p>14. Behavioural Regulation (Anything aimed at managing or changing objectively observed or measured actions)</p> <p>Constructs</p> <ul style="list-style-type: none"> • Self-monitoring • Breaking habit • Action planning 	X	<p><i>“...you had a pharmacist coming in and doing an audit on your over 65s every month, that they came in and had access to your system. I think it would be a great system.” (GP7)</i></p> <p><i>“We have started actually about 4 or 5 months ago, a repeat prescribing protocol within the practice and as part of that we look at STOPP/START.” (GP15)</i></p> <p>(STOPP/START: Screening Tool of Older Persons Prescriptions/ Screening Tool to Alert doctors to Right Treatment criteria)</p>

Important influences on GP prescribing behaviour identified using the TDF

Knowledge/Skills

Although they are described separately in the TDF, it was decided to merge the domains “Knowledge” and “Skills” as the findings that emerged were overlapping and therefore are reported as a single domain.

Participants reported the responsibility of prescribing for increasing numbers of complicated older patients as a burden. They voiced that they felt this would become even more demanding in the future. Participants reported a need to become more knowledgeable in pharmacology and drug interactions and they called for extra training in order to manage and treat these patients.

“... it’s going to have a huge impact on general practice and GPs, I think we’ll need to try and continue to improve our skills in that area and I think... care of the elderly ... will be a speciality ... it’s going to present a lot of challenges in terms of knowing the pharmacology and interactions.” (GP11)

Participants acknowledged the importance of their role as prescribers and suggested regular evaluation of their prescribing knowledge would motivate GPs to stay up-to-date with their prescribing skills and in some cases, change the way they practice or enhance the care of their patients.

“I personally think that we should have to every 6 or 12 months sit some kind of exam in prescribing ... because prescribing is so desperately important and I think the only way I would actually change the way I practice is if there was some kind of revalidation ...” (GP15)

Participants reported that they are influenced by information provided by pharmaceutical drug representatives despite viewing this information as biased. They called for alternative sources of succinct information that can be delivered in their practices, but is independent of the pharmaceutical industry and is evidence-based.

“Three times a week for 5 minutes I meet a drug rep ... so while we take it with a pinch of salt, because we know it’s biased ... we inevitably are influenced by drug reps ...”
(GP15)

Reinforcement Participants viewed prescribing in older people as a potential source of litigation should a prescribing error arise. They reported that the risk of error is higher in these patients due to the medical complexity and the possible interactions and side effects associated with the use of multiple medicines. The fear of litigation made some GPs more cautious and acted as an incentive to optimize their prescribing for these patients.

“I’m pretty sure it’s out there somewhere that it’s the biggest source of litigation I think for GPs is prescribing or ... prescribing errors.” (GP13)

Memory Attention and Decision Process

Participants actively considered various factors when prescribing medicines for example, when to start them, when to stop them, their side-effects, their potential for addiction, their potential adverse outcomes. The decision-making process can

become more complicated when a patient is already prescribed multiple medicines. This was mentioned as a particular issue when considering medicines with potential adverse effects, as they can lead to a prescribing cascade.

“If you do need to use something ... bearing in mind their cardiovascular risk, bearing in mind their falls risk that go with lots of the sedative medication, antipsychotics, sleeping tablets ... I think that’s my biggest bugbear, difficulty.” (GP13)

Some participants were reluctant to prescribe potentially useful medicines such as methotrexate out of fear of their side effects in older, more vulnerable patients. It was also evident that there was a level of caution and uncertainty around the prescribing of these high-risk medicines.

“But if it was something like methotrexate ... even thinking about it now would give you the heebee jeebees... you’ve somebody elderly in front of you and you’re really not sure, I just don’t think you can prescribe it really you know.” (GP11)

Environmental Context and Resources

Although prescribing was seen as an important responsibility by participants, they did not always get time to review medications as thoroughly as they would like.

“If you’re really busy sometimes and I’m just being honest, you just print off their last month’s prescription and you’ll keep going with that, you know.” (GP4)

Pharmacists were described as a useful resource for GPs especially in cases where older patients were having compliance issues with their medicines by dispensing

medicines into weekly/monthly blister packs. Reviewing prescriptions, checking drug doses and identifying potential drug interactions and side effects were other roles where pharmacists were identified as being a valuable support to the GP. Most participants reported a good working relationship with their local pharmacist.

“We’re very lucky that we have a very good relationship with the local pharmacist here they are very, very good and so we would be on to them a number of times a day ... particularly for people who come out from hospital whereas sometimes it isn’t clear what dose of medications they’re on.” (GP8)

Participants reported that GPs and pharmacists collaborate successfully together on a regular basis. However, it was suggested that the strengths of these existing relationships between GPs and pharmacists were not harnessed to their full potential. Maintaining and further enhancing the GP-pharmacist relationship was viewed as being an important strategy to improve prescribing and patient care.

“Pharmacists and doctors work very successfully together on a daily routine basis, and that’s probably not recognised enough but there is a significant interaction between the two. And anytime there’s good positive interaction you’ll always get positive responses and positive outputs.” (GP3)

Participants were asked to comment about the possibility of a service-orientated outreach educational intervention (such as academic detailing) provided by pharmacists to GPs in their surgeries. Participants welcomed the idea of an educational intervention delivered to individual practices rather than larger groups of GPs.

“It would probably be better to have a practice do it in isolation rather than two or three practices in the area doing it together. Because I’m not sure that all practices would like to be open with other practices about their prescribing. It’s kind of a personal thing, isn’t it?” (GP11)

Participants were asked about using information technology systems such as clinical decision support systems to help optimise their prescribing. They acknowledged that as prescribing is a complicated process especially in older people, computerised systems would be of some benefit but only to inform clinical situations and not to dictate them.

“... prescribing is so complicated in the elderly I’m not sure if a computer system could do it all. Now it might do a lot of it but at the end of the day you are still going to have to make a decision on the patient sitting in front of you.” (GP1)

Social influences

Participants reported that older patients can be influenced by the marketing of medications in the lay media. This can in turn influence patient requests and what GPs prescribe. For example, anticholinergic medicines are indicated for urinary incontinence, but GPs reported being reluctant to prescribe them for older people due to their side effects (i.e. falls, confusion and blurred vision). However, despite these reservations, GPs felt pressurised into prescribing these medicines due to patient expectations.

“... so people do present saying I saw the ad on the telly (for an anticholinergic medication for urinary incontinence) and I have the overactive bladder and you’re thinking anticholinergics and you’re 75 ... but they still expect it you know.” (GP1)

GPs experience difficulty in explaining why they are withholding such medications, particularly to an older person with hearing, visual or cognitive impairment. Stopping benzodiazepine medicines was another example of how patient preference conflicted with GPs’ knowledge about the risks of the medication.

“Any of those on the benzos you’d be trying to pull them all off it ... Very hard, very hard. And ... in spite of you talking about the risk of falls and obviously slowly weaning off ... but very hard to get patients off these tablets that are not essential really you know.” (GP7)

Social/Professional Role and Identity

Overall, the collaborative relationship between primary and secondary care was described as very good. However, some participants reported a lack of appreciation by their secondary care colleagues for their role as a GP. A lack of support from secondary care was highlighted especially with the management of complex patients in general practice.

“I think some of the hospital sector, don’t fully understand the nature of general practice ... I saw a person with a renal problem and I was in their house ... I rang the Urology (team) because they had a nephrostomy tube and they were asking me what

his creatinine was... they just had no idea that you don't have a portable creatinine monitor by your side ..." (GP8)

GPs described themselves as co-coordinators of care for patients, which was assisted by their detailed medical record for each of their patients.

"As a GP, you have a role as a co-ordinator of care, and you'd have the most up to date record of everything that's going on." (GP5)

Discussion

This study revealed the determinants influencing GP prescribing behaviour for older adults in primary care and GPs' views on potential intervention strategies to optimise prescribing for older often multi-morbid patients. A behaviour change theory was used to analyse the data and generate findings that could be used to inform intervention strategies.

The domain "Knowledge and Skills" highlighted that the responsibility of prescribing for increasing numbers of complicated older patients was viewed as a burden for GPs. This echoed the findings of a qualitative study of twenty practising general internists and family practitioners in the United States, which aimed to gain a deeper understanding of why they found caring for older patients so challenging. Three major domains emerged: medical complexity and chronicity for example, older people were seen to have more medical conditions, prescribed more medicines, be more vulnerable to illnesses and more susceptible to adverse drug reactions (ADRs); personal and interpersonal challenges for example, hearing problems, cognitive

impairment and family members caring for these patients, and, administrative burden for example, time consuming, increased workload, risk of litigation. Contextual conditions such as the practice environment and the GPs' training and personal values also influenced the care for these patients (157).

From the domain "Environmental Context and Resources" lack of available time for GPs was cited as a major barrier during clinical practice. As a result, GPs were unable to carry out all their clinical roles for example, review patient's monthly prescriptions upon renewal. Braddock *et al.* argue that the issue of time has an ethical significance as it may result in GPs sacrificing duties that promote important features of the patient-GP relationship such as trust, respect and fidelity, act as a barrier to shared decision making and being unable to fulfil their obligations as patient advocates (158).

Pharmacists were described as a reliable resource for GPs and many participants reported experiencing a good working relationship with their local pharmacist. In a qualitative study with 27 GPs and 31 pharmacists in the UK, GPs reported that knowing the pharmacist was an essential component of a successful GP-pharmacist collaboration. This professional familiarity was also considered an important factor in the provision of local pharmaceutical services pilots. Pharmacists experienced difficulty working in collaboration with large GP surgeries. GPs who were reluctant to collaborate expressed concerns about the standard of pharmacists' qualifications and therefore questioned their professional ability. Collaboration between both HCPs was optimised with reciprocal communication. Conversely, one-way communication was associated with lower levels of collaboration (159).

Implications for research and/or practice

Computerised decision support systems are widely used tools that optimise quality of care and patient outcomes (64). In practice, these systems may involve an alert system appearing at the end of a consultation or at the time of prescribing (9, 66, 160). Participants in our study agreed that computerised decision support systems could be a useful resource for GP prescribing, however some were concerned they may dictate rather than inform a clinical situation. In order for successful implementation of decision support systems in GP practices, software designers should consider the following: the system should be incorporated into the practice workflow and existing computerised systems, involve all stakeholders during various stages of the implementation process and ensure alerts are straightforward and easy to understand (161).

This study found that GPs feel they will need additional training in pharmacology and drug interactions as the older population increases. Prescribing for older people is a complex process and GPs welcomed supportive strategies to optimise the continuing care for this group of patients. One possible solution to optimise prescribing for this growing cohort of older patients prescribed multiple medications is academic detailing (AD). Academic detailers, who are usually pharmacists, nurses or doctors are trained to provide accurate, objective and up to date synthesis of the best available information on a clinical topic in an engaging format with GPs (162). This information often includes recommendations about alternative treatment regimens or non-pharmacological interventions (135). A pharmacist-led intervention

comprising AD demonstrated an improvement in statin prescribing in high-risk patients in primary care in the UK (137). A study in the United States found that two brief AD visits by clinical pharmacists to GPs reduced inappropriate prescribing by 14% in comparison with controls (163).

While clinical decision support systems and AD have been adopted in other countries these strategies are not routinely available in Irish general practice.

A large body of research has been carried out on the role of pharmacists in optimising GP prescribing in primary care. However, much of this work shows limited or inconsistent results. A Cochrane review examined the evidence for pharmacist-led interventions aimed at improving appropriate polypharmacy for older people across different healthcare settings. The authors concluded, based on the 12 studies included in the review, that it was unclear whether the interventions led to clinically significant improvements (112). Another systematic review focused on the effect of pharmacist-led interventions in optimising prescribing in older adults in primary care. Although it appeared that these interventions improved prescribing appropriateness, it was unclear if they resulted in clinically significant improvements in patient outcomes (59).

Despite these limited effects, our qualitative study shows that GPs still view the role of pharmacists and their own relationship with pharmacists in a positive way. It highlights that there is scope to harness the GP-pharmacist relationship to improve patient outcomes, and supports a need for intervention developers to consider other approaches to enhance the GP-pharmacist relationship in a way that will lead to meaningful and sustained improvements in prescribing.

Strengths and Limitations

The findings of this study are underpinned by a theoretical model that was specifically designed for analysing HCPs behaviour, and thus offers a number of strengths (150, 164). The TDF facilitates comprehensive assessment of the possible influences on behaviour, and, lends clarity to these influences by characterising each domain with component constructs. (150). However, the TDF is a relatively new framework and is still undergoing refinement. We suggest that future iterations of this framework may recognise the similarity between some domains in certain contexts such as “Knowledge” and “Skills” for cognitive tasks such as prescribing.

Prolonged engagement with the data was carried out as interviews were arranged with GPs over a five-month period, and were analysed on an iterative basis. The method developed by Francis *et al.* was used systematically to determine data saturation (153). Data triangulation was not conducted in this study as there was only one group of research participants. As GPs are the main prescribers of medication in primary care they were identified as the key participants to answer the study question. Also, one means of data collection was used that is, semi-structured interviews. This interview method was chosen as it has the ability to achieve comprehensive coverage of the topic discussed. The validation technique of member checking was not used (165), as returning interview transcripts to participants can lead to changes being made to the transcripts which can influence the trustworthiness of any subsequent analysis.

The transferability of the data may be limited by sampling GPs from one geographical region in Ireland. However, the broad inclusion criteria (requirement to be in active

practice) and the recruitment of GPs with a range of years of experience, gender, practice size and urban/rural locations may ensure that our findings reflect the most important factors that influence GP prescribing for older people in Ireland (166). Although data collection was only carried out by one researcher (D.O.R.), dependability was enhanced by using multidisciplinary team input for example, pharmacists (D.O.R., S.B., A.F.), GP (C.S.), physiotherapist (R.G.) and epidemiologist (P.K.) during data analysis (investigator triangulation). Additionally, D.O.R. maintained a reflective diary about his role and beliefs on the study topic during the course of the interviews and discussed this with other members of the team to help highlight any personal biases or challenges encountered.

Conclusion

This study has identified the key determinants that influence GP prescribing behaviour for older people in primary care. GPs are aware that prescribing for older people is a complex process that requires an increasing amount of their time and attention. GPs state that they require accurate, easily accessible sources of evidence-based data about the effectiveness and safety of treatments to support their prescribing for older, complex patients. Future interventions should incorporate means of providing such information, for example academic detailing (AD), to ensure that GPs are provided with necessary evidence and are equipped with the necessary skills to prescribe safely for the growing cohort of older complex patients.

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Chapter 6. Evaluating the feasibility of an academic detailing intervention with GPs in primary care: A mixed methods study.

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Abstract

Background

Academic detailing or educational outreach is a form of continuing medical education (CME) in which a trained health professional such a doctor or pharmacist visits prescribers in their practice to provide evidence-based information. While academic detailing has been adopted in Australia and the United States, this strategy is not routinely used in Ireland. The aim of this study was to assess the feasibility and acceptability of a pharmacist-led academic detailing intervention with a sample of practising GPs in Ireland.

Design and setting

A mixed methods feasibility study utilising quantitative data from patient medical records and qualitative focus groups with GPs in those ≥ 65 years with urinary incontinence in a region of Ireland.

Method

The intervention was delivered to GPs between June and September 2016. Qualitative focus groups were carried out with GPs who participated in the academic detailing intervention on urinary incontinence in older people. The focus groups were transcribed verbatim and analysed using thematic analysis. The medical records for all patients aged ≥ 65 years who were attending a participating GP with a diagnosis of urinary incontinence were retrieved and analysed using a before-after approach. The measures of prescribing assessed before and after the intervention were: LUTS-

FORTA criteria; Drug Burden Index; Anticholinergic cognitive burden scale; and the Screening tool of older person's prescriptions-screening tool to alert doctors to right treatment (STOPP/START) version 2 criteria.

Results

Twenty three GPs participated in the academic detailing intervention and 14 attended focus groups. Participants reported that this topic was relevant and practical to general practice. They described the educational materials as being of high quality, clearly presented and easy to follow. Participants appreciated the succinct nature of the information but would have preferred a more easily retrievable format, such as an online version rather than paper-based. The medical records of 154 patients were analysed. The mean age (\pm SD) of patients was 75 (7.2) years. The proportion of females was 72.1%. There was minimal or no change in any of the prescribing measures used.

Conclusion

This study demonstrated that a pharmacist-led academic detailing intervention was acceptable to GPs in a selection of different types of general practice in Ireland. Overall, participants highly valued the evidence-based approach of AD. The findings from this study will inform the planning and design of larger studies enhancing their likelihood of success.

Keywords: Academic detailing, older people, GPs, urinary incontinence, mixed methods, feasibility, primary care.

Introduction

The International Continence Society (ICS) has defined urinary incontinence (UI) as *“the complaint of any involuntary leakage of urine”* (167). It is a widespread medical problem that can cause a great deal of distress and embarrassment, as well as significant costs to individuals (168-170). More than 200 million people worldwide live with this condition. It is more common in women than in men due to a number of factors such as age, sex hormones, childbirth, hysterectomy, infection or other medical conditions (171). The severity of symptoms increases from middle age onwards (172). Despite the availability of evidence-based medicine, patients do not receive treatment because of their reluctance to report this condition or because for those in whom the condition is diagnosed are undertreated. In addition, when patients do seek help many doctors are not familiar with the latest information on the appropriate methods of evaluating and treating patients with this condition (173).

Academic detailing (AD) is an interactive, convenient and user-friendly approach to delivering non-commercial evidence-based medical information to healthcare professionals (163). This quality-improvement intervention, also referred to as educational outreach can be effective in changing prescribing practices, medical decision making and ultimately improving patient care (69). Academic detailers, who are usually pharmacists, nurses or doctors are trained to provide accurate, balanced and up to date syntheses of the evidence on a clinical topic in an engaging format with healthcare professionals in their work environment (174). The information provided often includes recommendations about non-pharmacological and other

treatment options and indicates where these options are appropriate (175). Several important principles are key to a successful AD program. These include defining clear and focused objectives, identifying participant's current knowledge and motivations, establishing credibility through a respected organisational identity and referencing evidence-based sources of information, using clearly presented graphic educational materials that are brief, engaging in two-way interaction, highlighting and re-emphasising key messages and reinforcing best practice with follow-up visits (68).

Previous studies have used a variety of methods to explore GPs experience of and satisfaction with AD in primary care. Frich *et al.* carried out focus group interviews to assess GPs and tutors experiences with peer group AD in Norway. It was reported that this educational approach was a suitable method to gain a better understanding of pharmacotherapy (176). Hartung *et al.* used short, written surveys to assess the effectiveness of and satisfaction with an AD pilot project with GPs in the United States. There was strong support and satisfaction among participants for the project. Participants preferred face-to-face approaches to distance interactions for example, video conference, online modules (174).

While AD has been adopted in other countries this strategy has not been tested as a sole intervention nor has it been adopted for use in Ireland. The OPTI-SCRIPT study (Optimizing Prescribing for Older People in Primary Care, a cluster-randomized controlled trial) was a complex, multi-faceted intervention conducted in primary care in Ireland. AD was one intervention component in this study. It involved a pharmacist carrying out a brief session with GPs discussing potentially inappropriate prescribing (PIP), a medicines review and web-based therapeutic treatment algorithms. The

results of this study were analysed using quantitative methods and demonstrated a reduction in PIP, particularly in modifying the prescribing of the proton pump inhibitors class of medicines (177). A further study reported a process evaluation of this intervention. Although participants reported their experience of the multifaceted intervention, the AD component was not discussed in detail (178). To date, no studies have evaluated the feasibility and acceptability of an AD intervention with GPs in Ireland using mixed methods research. The premise of a mixed methods approach is that the use of quantitative and qualitative methods in combination, provides a better understanding of research problems than either approach alone (179). Eldridge *et al.* have defined a feasibility study as a study asking “*whether something can be done, should we proceed with it, and if so, how*”. These studies are divided into three subgroups: randomised pilot studies; non-randomised pilot studies and feasibility studies that are not pilot studies (180). They are used to estimate important parameters that are needed to design larger studies for example, feasibility of recruitment, number of eligible participants and selection of appropriate outcomes (181). Therefore, the aim of this study was to assess the feasibility and acceptability of a pharmacist-led AD intervention with a sample of practising GPs using a mixed methods approach.

Methods

Study type

Creswell and Plano Clark have defined mixed methods research as a method that focuses on collecting, analysing, and mixing both quantitative and qualitative data in a single study or series of studies (179). In this study, a convergent parallel mixed methods design was used. The aim was to collect, analyse and interpret integrated quantitative and qualitative data to assess the feasibility of an AD intervention with GPs in primary care. The quantitative prescribing patterns of the GPs and their qualitative responses from the focus groups were brought together and compared. The underlying logic of this approach is that the integration of both qualitative and quantitative data is greater than each method's individual contribution (182, 183).

Convergent parallel design: the intent of the research is to collect both quantitative and qualitative data, analyse both datasets and then merge the results of the two data analyses with the purpose of comparing the results (Figure 6.1).

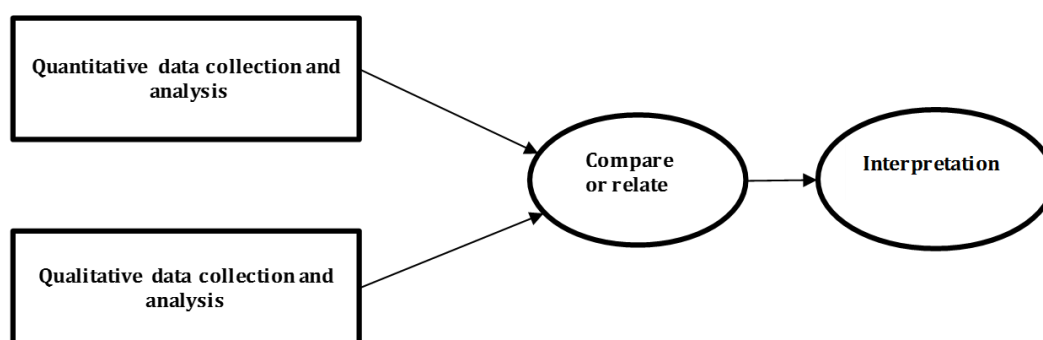


Figure 6.1 Convergent design

Setting

This study was carried out in six GP surgeries in County Cork, Ireland. The primary researcher (D.O.R.) arranged a meeting with the lead GP in each practice and a brief summary of the study was given. Other potential participants in each practice were contacted by telephone and invited to participate. Twenty three GPs participated in the intervention. All GPs who participated in the study received a certificate of participation and a certificate for their continuous professional development (CPD) (See Appendix IV).

Topic

The AD sessions were supported using material developed by the Alosa Foundation. The Alosa Foundation in Boston is a nonprofit organization and is independent of the pharmaceutical industry. It produces educational materials and decision making tools for Academic Detailers, and provides training on AD internationally (184). The Alosa Foundation granted the authors permission to use their educational material for this study (See Appendix IV). Prior to commencing GP recruitment, D.O.R. met with three GPs to discuss a topic for the AD intervention. From the list of 24 Alosa topics with a summary brochure the GPs chose urinary incontinence. They highlighted that this topic was not discussed regularly among themselves and currently their only source of information is provided by pharmaceutical drug representatives. Therefore the topic of urinary incontinence was used for the AD intervention with the GPs.

Academic detailing training

D.O.R. attended a two day AD training workshop at the National Resource Center for Academic Detailing (NaRCAD) in Boston, USA in May 2016. The workshop provided a critical foundation for the role as an academic detailer. It included sessions on the case for AD and evidence-based medicine, planning an AD visit, use of educational materials and role plays. This workshop helped to refine communication skills, improve clinical knowledge and gain confidence for attendees to carry out a successful educational visit.

Piloting the intervention

The AD intervention was piloted with three academic GPs in May 2016 before the study was launched. The GPs reported that they were very satisfied with this overall educational approach. The topic delivered and the educational materials used during the visit were also described as being very beneficial and relevant. The intervention was rolled out to participating GPs between June and September 2016. Figure 6.2 shows the timeline of the study.

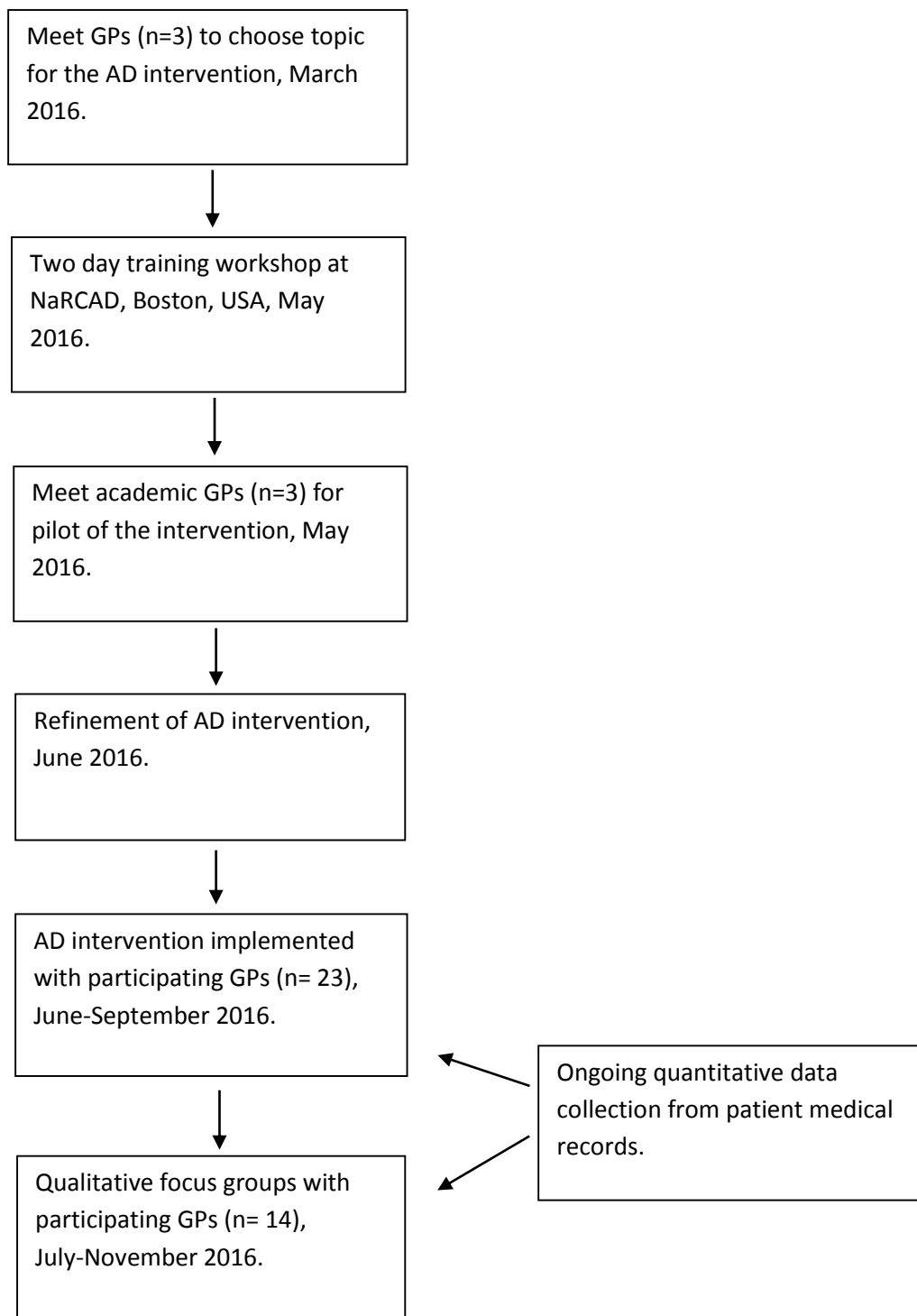


Figure 6.2 Timeline of the AD study

Qualitative method

Design

After the intervention was delivered to participating GPs by D.O.R., qualitative focus groups were conducted with GPs to explore its feasibility and acceptability. This interview method was chosen due to its ability to generate data by interaction between group participants. Participants can present their own views and can listen to the contributions from others in the group. This allows additional material to be triggered in response to what is reported by others. There was also a shared background to the research topic among the GPs (152).

Data collection

The primary researcher (D.O.R.) did not carry out the focus groups as this may have resulted in respondent bias from participants. D.O.R had also carried out a previous study with most of the participants and had developed a professional relationship with them. Therefore, the focus groups were carried out by other researchers (E.H.), (C.S.) and (S.B.) between July and November 2016. Four of the focus groups were carried out at the GPs surgeries during lunchtime and one was carried out at a meeting room in a nearby hotel after surgery hours. A topic guide was developed based on discussion and consensus agreement by all authors. It was iteratively refined after each focus group was transcribed and analysed to pursue emerging themes. Examples of the topic guide are provided as supplementary material to show its continuous development as the focus groups progressed (Appendix IV). The focus

groups were audio-recorded. All researchers recorded field notes immediately after each focus group and this facilitated preliminary familiarisation with emerging themes.

Analysis

All focus groups were anonymised and fully transcribed and saved in QSR International's NVivo Qualitative Data Analysis Software (V.10.22) to facilitate analysis (185). The descriptions of GPs' views were analysed using thematic analysis. This approach was used as it provides a flexible and useful research tool, which can potentially provide a rich and detailed account of the data (186). It consists of six phases of data analysis (186). The first phase involved several readings of the interview transcripts to ensure familiarity with the data. The second phase involved generating initial codes. The next phase which refocuses the analysis at the broader level of themes involved sorting the codes into potential themes. The fourth phase involved a refinement of the candidate themes. The fifth phase involved defining and naming themes. The last phase began with a set of clearly defined themes and involved final analysis and write-up. To enhance the credibility of the coding, three members of the research team (D.O.R., C.S. and S.B.) independently coded a sample of the transcripts.

Quantitative method

Study population

This was an analysis of patient medical records (PMRs). All patients aged ≥ 65 years with urinary incontinence treated by GPs who participated in the AD study were

included. D.O.R. analysed their medical records at multiple time points before and after the intervention (six and three months before the intervention (T_{-6}), (T_{-3}), at the time of the intervention (T_0) and three and six months after the intervention (T_3), (T_6). Community-dwelling patients aged ≥ 65 years with urinary incontinence were identified by searching GP databases and notes. D.O.R. recorded the following patient information using Microsoft Office Excel[®] (2013), patient demographics (age, sex, medical card status and smoking history), body measurements (blood pressure [systolic and diastolic], cholesterol, weight, body mass index (BMI)) chronic prescription medicines and medical history.

The following criteria were applied to the patient data recorded:

LUTS-FORTA criteria

Drugs to treat lower urinary tract symptoms (LUTS) regularly used in older people aged ≥ 65 years are classified on their appropriateness based on efficacy, safety and tolerability using the Fit fOR The Aged (FORTA) criteria. This criteria classifies drugs for the treatment of LUTS into four ordinal categories, A (absolutely: indispensable drug), B (beneficial: drugs with proven efficacy), C (careful: drugs with questionable efficacy/safety profiles) and D (don't: avoid in older people) (49).

The Drug Burden Index (DBI)

The DBI was developed to measure the cumulative exposure to anticholinergic and sedative medicines in older people and its impact on physical and cognitive function

(50). The calculation of the DBI is based on a pharmacological equation that incorporates drug dose and the principles of dose response (51).

$$DBI = \sum D / \delta + D$$

D is equal to the daily dose taken and δ is the recommended minimum dose recommended by a relevant formulary (50). For each drug the DBI ranges from 0-1, with 0 being no burden, 0.5 being exposure to the minimum daily dose and upwards to 1 as the dose is increased exponentially (52). The sum of these individual drugs (anticholinergic/sedative drugs) equals to the total drug burden. In this study, the list of drugs with clinically significant anticholinergic and sedative effects were defined from a composite list developed from a review by Duran *et al.* 2013, the anticholinergic cognitive burden scale developed by Boustani *et al.* 2008 and from a study published by Ailabouni *et al.* 2017 (56, 187, 188) . This composite list consisted of 133 drugs. The minimum geriatric dose of drugs were obtained from the British National Formulary Edition 71 (BNF) and reconciled with the drug Summary of Product Characteristics (SPC) as listed by the Health Products Regulatory Authority (HPRA) in Ireland (189).

Anticholinergic cognitive burden scale (ACB)

The cumulative effect of taking multiple medicines with anticholinergic properties is defined as the anticholinergic burden (53). Previous studies have demonstrated that the use of medicines with anticholinergic activity among older adults is associated with physical and cognitive decline (54, 55). The ACB is based on a systematic

literature review of medicines with known anticholinergic activity. The scale consists of 88 drugs with known anticholinergic activity and assesses individual drugs that have none, possible or definite anticholinergic properties with a score ranging from 0 to 3. A cumulative score is generated if a patient is on multiple anticholinergic medicines (56).

STOPP/START version 2 (V2) criteria

An explicit screening tool was used to capture the prescribing appropriateness and compare it with other study populations within the thesis. Prescribing inappropriateness was assessed using The Screening Tool of Older Persons Prescriptions, Screening Tool to Alert doctors to Right Treatment (STOPP/START) criteria, a validated and explicit measure of potentially inappropriate prescribing (PIP) and potential prescribing omissions (PPOs) for use in older adults (≥ 65 years) in European countries (76). In 2014, the criteria were revised and updated. The revised set, STOPP/START version 2 (STOPP/START V2), consists of 80 STOPP and 34 START criteria (40). A subset of the criteria (62/80 STOPP, 22/34 START) were applied as some were not relevant to the data collected for example, the administration of vaccines. (See Appendix IV).

D.O.R. applied the LUTS-FORTA, DBI, ACB and STOPP/START V2 criteria to patient related data retrieved from the electronic medical records. For validation purposes, the four types of criteria were applied independently by a second member of the research team to a random 10% sample of the data.

Outcomes

The four outcomes of interest were the overall prevalence of LUTS-FORTA, DBI, ACB and PIP/PPOs in the patients.

Statistical analysis

Data analyses were performed using STATA[®] version 13 (StataCorp, College Station, Tx, USA). Continuous variables were presented as mean with standard deviation (SD) and range, or median with interquartile range (IQR), as appropriate, and categorical variables as frequency (percentage). It is important to note that a feasibility study is not a hypothesis testing study (190). One of the key aspects of these studies is that they do not evaluate effectiveness as they are not powered to do so (191). The main focus of this feasibility study was to assess feasibility of the intervention, therefore the data were analysed using descriptive statistics. Statistical testing was not undertaken as the study did not aim to draw inferences from the data (192). However, this data may be informative for researchers planning similar work or planning definitive intervention studies (i.e. trials).

Standardised reporting guidelines

The Good Reporting of a Mixed Methods Study (GRAMMS) framework was used to inform reporting of the findings (193, 194). (See Appendix IV)

Ethical approval

Ethical approval for this study was granted by the Clinical Research Ethics Committee of the Cork University Teaching Hospitals, Cork (reference ECM 4 (s) 10/05/16 & ECM

3 (ddddd) 07/03/17) and the Mallow Primary Health Centre (MPHC), Cork ethics committee (See Appendix IX).

Results

Qualitative results

Five focus groups were conducted in total. The focus groups ranged from 19 minutes to 48 minutes (median interview length (minutes), interquartile range (IQR), 21 (20, 24)). The mean duration of medical experience of GPs' that participated in the focus groups was 21 years (range 0 to 42). The number of GPs working in a practice ranged from 1 to 7. The characteristics of GPs interviewed are detailed below (Table 6.1).

Table 6.1 Characteristics of GP participants in the focus group

General Practitioner (GP)	Gender	Years of medical experience	No of GPs in the practice	Participant number in focus group	Focus group number
1	M	27	4	1	1
2	M	6	4	2	1
3	M	35	5	3	1
4	M	38	7	4	1
5	M	42	7	5	2
6	M	0*	7	6	2
7	M	29	4	7	3
8	F	1	5	8	3
9	F	22	4	9	3
10	M	24	7	10	4
11	F	1	7	11	4
12	F	21	1	12	5
13	F	20	2	13	5
14	M	22	2	14	5

*GP registrar

Themes

Theme 1: The academic detailing experience

Subtheme: Convenience of academic detailing

Participants highlighted the convenience of the AD session being carried out in their working environment. They welcomed this educational visit being delivered with little disturbance to their daily practice. They also reported that they are prepared to block out some of their working time to accommodate this source of evidence-based information.

“The whole process of somebody coming to the practice to somewhere like this, to a small group complements the brevity and concise nature of it and kind of the convenience in that respect of it is good. You can slot it into your day ...and if you’re looking at trustworthy information presented in a similarly available kind of way, you are far prepared to... put 15-20 minutes of your time aside to kind of look at this.”

(GP2 Focus group 1)

This was in contrast to the alternative sources of evidence-based information that are currently available for GPs. Participants reported the frustration at not being able to attend courses of interest due to the demands of their work schedule.

“I mean it’s very hard. Even though you’d see stuff that might be on, it could be on a Saturday but you know you could be working Saturday surgery, it’s hard to attend everything so.” (GP11 Focus group 4)

Subtheme: The interaction

Participants described the interaction between the GP and the academic detailer as being important to the success of the intervention. They reported that the session worked because it felt relaxed and free of pressure. This was in contrast to their experience with some pharmaceutical drug representatives who they described as having an aggressive approach combined with an overload of information, which seemed to aggravate participants.

*“Relaxed, it wasn’t a, you didn’t feel pressurised. Sometimes when you get drug reps in they are selling. It’s a different conversation...I want you to prescribe my Tolterodine, or my Mirabegron or my, whatever you know. Where I’m going to tell you the forty reasons why and then I’m really going to p*** you off by pulling out something that you don’t want to see and I’m going to give you a study that we have produced.” (GP10 Focus group 4)*

Subtheme: The educational materials

Participants said they liked the educational materials because they had a clear layout and were easy to follow. They reported that they valued the succinct nature of the key messages while the tables and figures were presented in a straightforward way.

“First of all, well presented, clear, succinct, easy to read... and it got to the core messages quite well and it wasn’t over graphed or over too much stats, things that distract me. I thought it was quite well done.” (GP7 Focus group 3)

Subtheme: The topic: Urinary incontinence

Participants reported a desire to become more knowledgeable in urinary incontinence however, it was not a topic that they seek out themselves.

“It’s something that you would like to know more about. It’s never on your radar to actually go out and read an article on overactive bladder.” (GP1 Focus group 1)

The topic of urinary incontinence was agreed by a number of GPs prior to rolling out the study. Participants reported that this topic was relevant and suitable to general practice. The relevance of this topic facilitated the delivery of the intervention to GPs.

“I think this worked well cause we had input in actually what the topic was. So effectively it was something that would have been relevant and applicable so immediately that makes you less resistant.” (GP1 Focus group 1)

Theme 2: Behaviour change

Participants were asked whether this type of educational intervention would change their behaviour. They highlighted the importance of engaging with the academic detailer during the visit in order to optimise the possibility for behaviour change.

“I would think the more input you have into it yourself, if somebody just comes in and talked to you and you’ve put nothing into it I don’t think it’s going to change anything.” (GP12 Focus group 5)

Participants described the likelihood of changing their behaviour in treating patients with urinary incontinence following the intervention. However, this change in behaviour could be influenced by environmental resources such as the availability of primary care physiotherapists.

“Oh I’d say I’d change a bit you know. Provided you see that, stuff like physios and that kind of a thing are available but they’re not.” (GP5 Focus group 2)

Subtheme: Knowledge gained

Participants were asked if they had gained any knowledge from the intervention. Some participants were not aware of the important role that non-pharmacological methods play in treating urinary incontinence. These methods are often recommended first line and can be very effective in managing this condition.

“Yeah I learned a lot... I didn’t realise that the non-pharmacological methods would be as good or better than the pharmacological methods ... to use them as your first line and only when a failure of... kegel muscle exercises, or ... bladder diaries and only when that fails would you go to pharmacological treatment. I thought that was interesting.” (GP6 Focus group 2)

For some participants, the intervention served to refresh their knowledge with the topic rather than gain new knowledge as some of the treatment options may be more commonly used than others.

“I suppose it more refreshed my knowledge of it rather than gave me new knowledge so it just made me more aware of the treatment options that were there, some come on your radar and some come off your radar over time.” (GP14 Focus group 5)

Theme 3: Sustainability

Subtheme: Academic detailing ownership

Participants were asked how this type of educational intervention could be rolled out to a wider group of GPs in Ireland. Some suggested that it could be affiliated with the Irish College of General Practitioners (ICGP), the professional and educational body for general practice in Ireland. The association with this recognised body could enhance the credibility of AD among GPs.

“I think if it can be affiliated with the Irish college it would probably be more important being honest because that gives a bit of a imprimatur and it kind of gets people more receptive to it because if the Irish college are involved and they’ve tailored it to general practice...” (GP 14 Focus group 5)

However, some participants were reluctant for regulatory bodies such as the Health Information and Quality Authority (HIQA) being involved.

“Not HIQA.” (GP11 Focus group 4)

“Not HIQA. Don’t mention that word here.” (GP10 Focus group 4)

Subtheme: Online educational material

Participants suggested an online version of the educational material, which would be easier for them to manage in a setting where print materials over-accumulate or go missing.

“I think an online pack is a good idea, even like relevant, like I know he gave us the cards but you see the cards, where do you put the cards, you can’t stick up every card all over your wall but you need something that just pops up in front of you, so even if there is a handy pack literally with the summary page and you know advised drugs.”

(GP11 Focus group 4)

Subtheme: Advance notice of the visit

Participants suggested that advanced notice of the visit could help to optimise the AD session with the detailer. This would give the GP the chance to prepare for the visit by thinking about how they manage their patients regarding the topic or information related to the latest treatments.

“If you know someone is coming in say on a Thursday. On a particular topic. You certainly think of patients coming in to you and you know that kind of focuses you a little bit so yeah I think that would probably be good. Even an email or a just a reminder ... that this is happening and anything that you may want to consider in relation to difficult patients to treat or other things, newer treatments or whatever.”

(GP 14 Focus group 5)

Subtheme: Desire for practice staff involvement

Participants highlighted the importance of incorporating the wider members of the practice team in the AD sessions. This is especially significant given the expanded role of nurses in primary care.

"I'd be quite keen to involve the practices nurses... because they, say with urine incontinence, with lots of other topics... patients ...sometimes tell nurses things that they don't tell doctors ...realistically long term they're going to be doing an awful lot of the chronic disease management sort of stuff...". (GP14 Focus group 5)

Subtheme: Participation format

Participants were asked whether these educational sessions should be delivered one-to-one or in a group setting. They suggested that group sessions would work well as GPs might also then learn from each other, however group sessions were not tested in this study.

"Small group I'd say works well. You might get more relevance out of a small group and that the interaction between people and different emphasis and that type of thing. I think that interaction leads to more learning anyway." (GP3 Focus group 1)

However, some participants said they viewed the one-to-one format as preferential as it facilitates greater information exchange between academic detailer and prescriber. They also felt that one-to-one sessions were less susceptible to distractions.

"When you are together with the presenter you get much more information and you are really focusing on what he's speaking compared to when you are in a group." (GP8 Focus group 3)

Participants were asked if they would be interested in participating in future AD studies. All indicated a willingness to do so.

"Yes very interested." (GP9 Focus group 3)

“Yeah, I would absolutely yeah.” (GP11 Focus group 4)

Quantitative results

The characteristics of 154 patients diagnosed with urinary incontinence included in the study are detailed in Table 6.2. The mean age (\pm SD) of patients was 75 (7.2) years. The proportion of females was 72.1%. The median number of drugs (IQR) prescribed to patients was 7 (5, 10). The proportion of patients with urge incontinence was 32%. The documentation of Pelvic floor muscle training (PFMT) was reported in 15% of PMRs at one time point in the study (T₆).

Table 6.2 Baseline characteristics

Population characteristics	Total (n=154)
Mean age (years) (\pm SD), range	75 (7.2), 65-93
Female, n (%)	111 (72.1)
*GMS medical card holder, n (%)	122 (79.2)
Current smokers, n (%)	7 (4.5)
Mean blood pressure (\pm SD)	136/76 (17.1/10.3)
Mean total cholesterol (\pm SD)	4.8 (1.1)
Mean BMI (\pm SD)	28.1 (4.9)
Median number of drugs prescribed per patient, interquartile range (IQR)	7 (5,10)
Median number of all comorbidities per patient, interquartile range (IQR)	6 (4,9)
Type of incontinence	
Stress,	13 (8%),
Urge,	49 (32%),
Mixed,	24 (16%),
Unknown, n (%)	68 (44%)

*GMS (General medical services) is a means-tested scheme that entitles those who qualify to have access to public health services, free of charge.

LUTS-FORTA score

Figure 6.3 shows the LUTS-FORTA score in patients over time. According to the criteria, no drug was rated in category A. Patients prescribed drugs in category C showed an increase over time, while patients prescribed drugs in category B and D showed no change. Appendix IV shows the drugs that were identified by the LUTS-FORTA criteria.

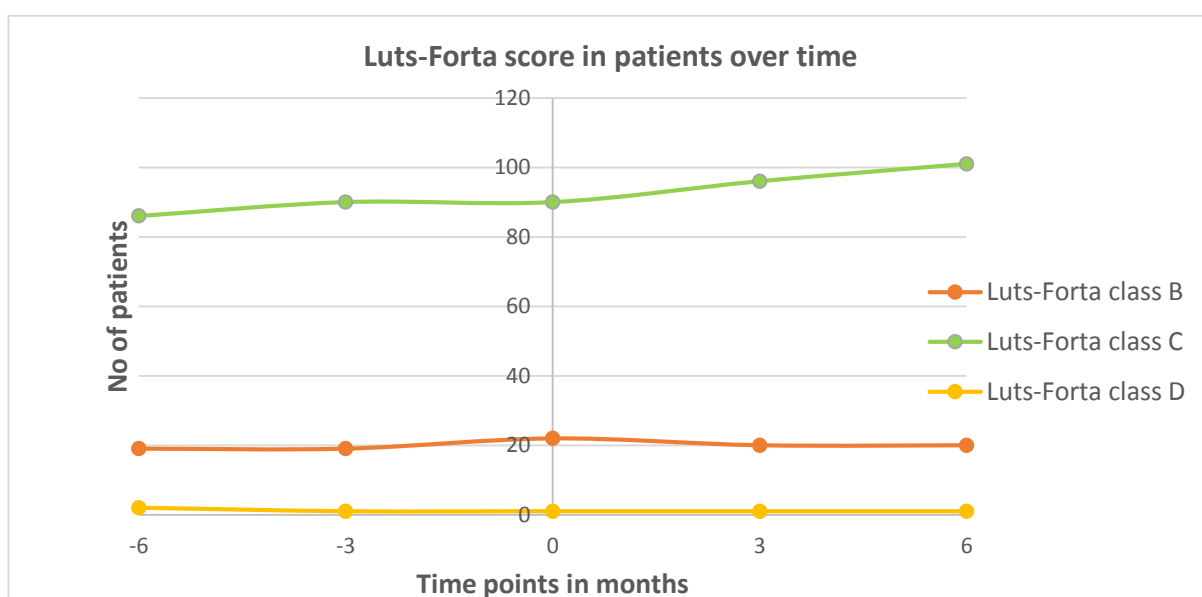


Figure 6.3 The LUTS-FORTA score in patients over time

Drug Burden Index

Almost 65% (100/154) of patients did not show any change in drug burden over time. While, 14% (21/154) showed a decrease in DBI score and 21% (33/154) showed an increase. Table 6.3 shows the DBI score in patients over time.

Table 6.3 DBI score in patients over time

DBI score	T ₋₆ n (%)	T ₋₃ n (%)	T ₀ n (%)	T ₃ n (%)	T ₆ n (%)
No burden	36 (23)	31 (20)	31 (20)	31 (20)	27 (18)
0.01 to 0.5	29 (19)	28 (18)	30 (20)	28 (18)	31 (20)
0.51 to 1.0	32 (21)	37(24)	35 (23)	33 (21)	31 (20)
More than 1.01	57 (37)	58 (38)	58 (38)	62 (40)	65 (42)

Anticholinergic cognitive burden (ACB) scale

Figure 6.4 shows the ACB score in patients over time. This scale assesses individual drugs that have none, possible or definite anticholinergic properties with a score ranging from 0 to 3. In this study some patients received a score of 4 or more. Thirty-four per cent of patients at T₋₆ months and 31% of patients at T₆ months had an ACB score of 0. Twenty five percent of patients had an ACB score of zero at the start and end of the study (T₋₆, T₆). The number of patients with ACB scores of 1, 4 and ≥5 showed an increase from the time of the intervention (T₀) up to three (T₃) and six (T₆) months after.

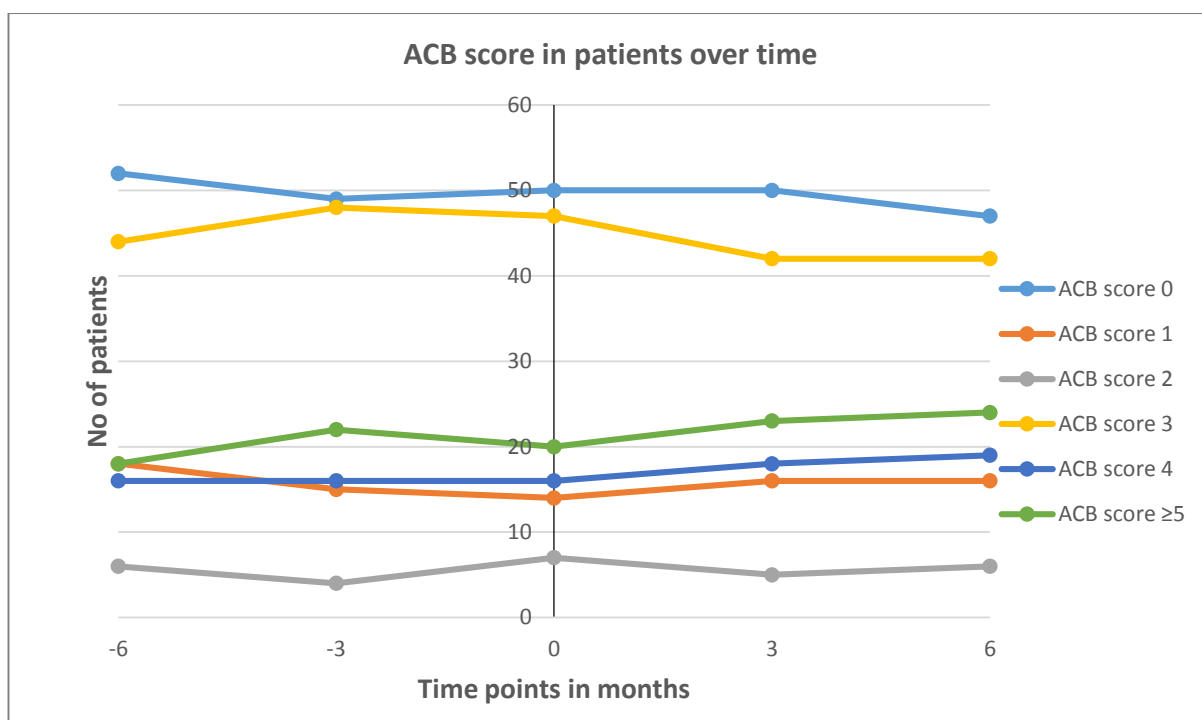


Figure 6.4 The ACB score in patients over time (n=154)

STOPP/START

Table 6.4 shows the overall PIP/PPO prevalence and the most common examples of PIP and PPO throughout the study. The overall prevalence of PIP/PPOs was defined as the proportion of participants having at least one PIP or PPO according to the STOPP/START V2 criteria among all participants included in this analysis. The overall prevalence of PIP changed from 37% at T₋₆ to 39.6% at T₆ (95% CI -0.1-0.01). The overall prevalence of PPOs changed from 30.5% at T₋₆ to 27.9% at T₆ (95% CI -0.01-0.1). Approximately 51% of patients did not have any PIP/PPO issues at T₋₆, while 50% of patients did not have any PIP/PPO issues at T₆. The most frequent PIP in patients were any drug prescribed beyond the recommended duration; the prescribing of benzodiazepines and the prescribing of hypnotic Z-drugs. The most frequent PPOs in patients were vitamin D and calcium supplements in patients with osteoporosis;

Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease and laxatives in patients receiving opioids regularly.

Table 6.4 PIP/PPO prevalence and the most common examples of PIP and PPO throughout the study

Timeframe (Months)	PIP prevalence (%)	PPO prevalence (%)	Most common PIP (%)	Most common PPO (%)
T ₋₆	37.0	30.5	1. STOPP 2 A2 (11.0) 2. STOPP 2 K1 (9.7) 3. STOPP 2 K4 (9.7)	1. START 2 E3 (9.1) 2. START 2 A6 (8.4) 3. START 2 H2 (7.8)
T ₋₃	37.0	29.2	1. STOPP 2 A2 (11.0) 2. STOPP 2 K1 (9.7) 3. STOPP 2 K4 (9.7)	1. START 2 E3 (7.8) 2. START 2 A6 (7.8) 3. START 2 H2 (6.5)
T ₀	37.7	28.6	1. STOPP 2 A2 (11.0) 2. STOPP 2 K4 (10.4) 3. STOPP 2 K1 (9.7)	1. START 2 E3 (8.4) 2. START 2 A6 (7.8) 3. START 2 H2 (6.5)
T ₃	40.9	27.9	1. STOPP 2 K4 (11.7) 2. STOPP 2 A2 (10.4) 3. STOPP 2 K1 (9.1)	1. START 2 E3 (7.8) 2. START 2 A6 (7.1) 3. START 2 H2 (7.1)
T ₆	39.6	27.9	1. STOPP 2 K4 (11.7) 2. STOPP 2 A2 (10.4) 3. STOPP 2 K1 (9.1)	1. START 2 E3 (7.8) 2. START 2 A6 (7.1) 3. START 2 H2 (7.1)

STOPP2 A2: Any drug prescribed beyond the recommended duration, where treatment duration is well defined; **STOPP2 K1:** Benzodiazepines; **STOPP2 K4:** Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon. **START2 E3:** Vitamin D and calcium supplements in patients with known osteoporosis; **START2 A6:** Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease; **START2 H2:** Laxatives in patients receiving opioids regularly.

Discussion

This study used a mixed-methods approach to 1) qualitatively explore the feasibility and acceptability of an AD intervention among GPs in primary care and 2) quantitatively evaluate the ability of measuring an impact of the intervention.

A feasibility study that is not a pilot study was used in this research. They are defined as studies in which researchers attempt to identify whether an element of the future trial can be performed but do not implement the intervention to be evaluated or other systems to be undertaken in a future trial, although intervention development may be addressed in some way (180).

The prescribing outcomes LUTS-FORTA, DBI, ACB and STOPP/START V2 criteria were described over the study time points. Drugs in category C of the LUTS-FORTA score showed a slight increase over time, while those in categories B and D showed no change. Regarding the DBI, the majority of patients showed no change in drug burden over time. The number of patients with ACB scores of 1, 4 and ≥ 5 increased from the time of the intervention (T_0) until the end of the study. Although the prevalence of PIP and PPOs was high in this study, the prevalence of both outcomes did not change dramatically over the different time points. The involvement of GPs in the choice of topic was seen to be a key factor in the success of the intervention. However, although some participants from the focus groups reported a desire to become more knowledgeable on urinary incontinence, they also highlighted that it was not a topic that they actively seek out. Urinary incontinence may not have been high on their list of priorities compared to topics such as cardiovascular disease or diabetes. This may be reflected in the minimal change in measures of prescribing assessed in the study.

Participants also described the possibility of behaviour change following the intervention however, this was dependent on the availability of primary care resources such as physiotherapists. In Ireland, GMS patients are often on a waiting list to attend primary care physiotherapists. PFMT is an effective treatment for women with urinary incontinence and these exercises are often demonstrated by physiotherapists. If there is a lack of these healthcare professionals then GPs may have no option but to treat patients with medicines. This can increase the prescribing cascade if patients are already on multiple medicines. PFMT was reported in 15% of PMRs at one time point (T₆) in the study. Participants described the educational materials as being high quality. These materials contain evidence-based information on the prevalence of urinary incontinence, an overview of the interventions and cost of drugs to treat the condition and key messages which may be very beneficial for GPs. However, if this information is not easily retrievable for GPs then they may not be used as a treatment resource during a patient consultation. This may have limited the change in prescribing outcomes in the study. Participants called for these materials to become available as an online resource as they could be of value in optimising the diagnosis and management of urinary incontinence.

Comparison with existing literature

Allen *et al.* used a mixed methods study (a questionnaire and semi-structured telephone interviews) to explore family physician perceptions of AD and the factors that affect their use. Several factors were identified that encourage the use of AD. They were, the relevance of the topic, the evidence-based approach adopted and the

educational material used (195). These findings are similar to those in our study. The GPs selected the topic of urinary incontinence for the intervention and described it as relevant. They welcomed the idea of evidence-based information being presented to them in their practice and they also described the educational material used as being of high quality. Soumerai recommends that educational materials should be brief and clearly presented (68). In this study a one-to-one detailing model was used. However, participants reported that they would be willing to participate in small group detailing. Evidence suggests this format of detailing is effective at optimising prescribing. Van Eijk *et al.* showed that individual and group AD visits improved the prescribing appropriateness of anticholinergic depressants (196). However, Figueiras *et al.* found that the one-to-one format was more effective than group education at improving the prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) (197). Participants reported that the more input they had into the session the more likely it would change their behaviour. They also reported that environmental factors would also influence their behaviour. Hartung *et al.* found that clinicians who participated in face-to-face detailing reported a higher likelihood of changing their behaviour (174). For this intervention, all GPs received one visit from the detailer, however research has indicated that frequent reinforcement visits can optimise behaviour change (198). In this study, GPs indicated a willingness to participate in future AD studies. Hartung *et al.* also reported similar findings (174). Habraken *et al.* highlighted that Belgian physicians highly rated AD visits and approximately 90% of those surveyed were willing to use this service again (70).

The measures of prescribing assessed: the LUTS-FORTA, DBI, ACB and STOPP/START showed minimal or no change in their scores following the intervention. However, it is important to highlight that this study was not designed or powered to demonstrate effectiveness. Also the key focus of this study was to optimise the diagnosis and management of urinary incontinence and not to change the impact of prescribing. Other AD studies have evaluated efficacy. A cluster randomised, stepped-wedge trial consisting of an AD component of a complex intervention reduced the rate of high risk prescribing of antiplatelet medicines and NSAIDs in the UK (199). A randomised control trial carried out in the United States found that two face-to-face visits by clinical pharmacists to GPs reduced inappropriate prescribing by 14% compared to the control group (200).

Strengths and limitations

The qualitative data supplemented the quantitative data by identifying convergence and divergence between the two datasets (179). The information extracted from the PMRs for example, patient demographics, co-morbidities and medication facilitated a comprehensive analysis of the prescribing outcomes. To enhance the validity of the quantitative results, a sample of the data were independently reviewed by two healthcare professionals. The focus groups were arranged with GPs over a five-month period and this facilitated prolonged engagement with the data. Qualitative data collection was carried out by three researchers (E.H., C.S. and S.B.) and dependability was enhanced by using a multidisciplinary team input for example, pharmacists, GP, physiotherapist and epidemiologist during data analysis.

Although 23 GPs participated in the intervention only 14 were available to attend the focus groups. All participating GPs were contacted in advance about the focus groups, however, some were on holidays on the scheduled date while others who agreed to participate had to cancel at the last minute due to time constraints during work or emergency situations that arose with patients. There was no control group used in the study and as a result this limited the comparison between the GPs who received the intervention and those who didn't.

The findings from this study may be beneficial to other researchers when developing their own study designs as they may enhance their approach or avoid similar pitfalls (201). Future studies could evaluate the impact of newly diagnosed incontinence patients with an intervention and control group. A follow up visit could be arranged with the GPs after four to six weeks to reinforce the key messages from the first visit and to identify if they have been successfully implementing any suggested changes. It would also give the academic detailer an opportunity to answer any additional questions that the GPs may have. Qualitative work could also be carried out with Urologists to identify their views on the management of urinary incontinence in primary care. Although the academic detailing training took place in the United States, a "train the trainer" approach could be utilised to make it more feasible for an Irish context. Instructors could train their colleagues and this would help to build a pool of competent academic detailers. Finally, large randomised control trials that have clear objectives, explicit criteria, are methodologically robust and have a long duration of follow-up should be considered.

Conclusion

This mixed-methods study explored the feasibility and satisfaction of a pharmacist-led AD intervention with GPs. Overall, participants highly valued this evidence-based approach and welcomed further visits. Selecting a relevant topic was considered important. The printed educational materials were reported as being of high quality, however an online version was preferred. Although there was minimal or no change in the measures of prescribing assessed, we believe that publishing these results are important for researchers planning similar studies. Further research is needed in a larger population evaluating the impact and cost effectiveness of AD to optimise patient care.

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Chapter 7. Discussion

The overall aim of this thesis was to understand the potential role of the pharmacist in optimising prescribing for older people in primary care.

This chapter highlights the findings from each individual chapter to create an overall summary of the evidence. Firstly, Chapter 3 sets the scene by highlighting the prevalence of PIP and PPOs across three European countries. Secondly, Chapter 4 summarises the evidence of pharmacist-led interventions in optimising prescribing in older adults in primary care. Thirdly, Chapter 5 reveals the determinants of GP prescribing behaviour for older adults in primary care and elicits GPs' views on the potential role for broad intervention strategies involving pharmacists and/or information technology systems in general practice. Finally, these findings have informed the pharmacist-led academic detailing (AD) intervention with GPs in Chapter 6. The feasibility of this study was evaluated using a mixed methods approach. The strengths and limitations of the thesis are explained. The policy implications of the thesis findings are also outlined in addition to highlighting areas for further research.

7.1 Summary of findings for the cross-sectional study

This study estimated and compared the prevalence and type of PIP and PPOs amongst community-dwelling older adults (≥ 65 years) in three European populations using STOPP/START V2 criteria. Overall, the prevalence of PIP was 12.9% ($n=69$) and was similar in the Irish, Swiss and Dutch participants. The overall prevalence of PPOs

in the three populations was 22.2% (n=118) and was higher in the Swiss and Dutch than in the Irish participants. Participants at the Swiss and Dutch sites were at increased odds of any PIP and PPOs after adjusting for age, sex, multimorbidity and polypharmacy compared to participants at the Irish site. A greater understanding of PIP was gained from this study by highlighting its prevalence across three European populations. This study also offered the opportunity to compare the characteristics of trial participants recruited by sites in different countries, and to compare prescribing behaviours internationally. For example, the prescribing of benzodiazepines in Ireland was lower compared to Switzerland and the Netherlands. The use of national benzodiazepine audits, with individual practice feedback, may have optimised the prescribing of these medicines among Irish GPs (89). This study also described the role of the GP across the three countries. Therefore, by highlighting and comparing the prevalence of prescribing issues, this study illustrated the need to identify a potential pharmacist-led intervention to optimise prescribing appropriateness in older people in primary care.

7.2 Summary of findings from the systematic review

This review systematically evaluated studies of pharmacist-led interventions on potentially inappropriate prescribing among community-dwelling older adults receiving primary care to identify the components of a successful intervention. Five studies met the inclusion criteria. Four studies involved a pharmacist conducting a medication review and providing feedback to patients or their family physician. One RCT evaluated the effect of a computerised tool that alerted pharmacists when

elderly patients were newly prescribed potentially inappropriate medications (PIMs). Four studies were associated with an improvement in prescribing appropriateness. Overall, it demonstrated that pharmacist-led interventions may improve prescribing appropriateness in community-dwelling older adults. However the quality of evidence is low.

In an update of this systematic review conducted in May 2017, two additional studies were found, the results of which were consistent with the previously included studies, and thus did not change the conclusion of the review. Haag *et al.* evaluated the impact of a pharmacist-provided telephonic medication therapy management (MTM) on care quality in a care transition program (CTP) from a hospital to home for high-risk older adults. In this prospective, randomised, controlled study, patients were randomised to the pharmacist intervention or usual care which consisted of a nurse practitioner reviewing the patient's medications. The primary outcome was to identify PIP and PPOs using STOPP/START V1 criteria. No significant differences were found between the two groups in medicines using the criteria. The small sample size of the study (n=25 patients) may have limited the possibility of detecting a difference between the groups (202). Campins *et al.* assessed the safety and effectiveness of a pharmacist-led medication evaluation programme for community-dwelling polymedicated (≥ 8 medicines) older people. The pharmacist review of medications included recommendations to the patient's physician. This was a randomised, open-label, multicentre, parallel-arm clinical trial with a one year follow-up that used the STOPP/START V1 criteria to assess medication appropriateness. The control group patients received the usual standard of care from their physicians. Approximately

26.5% of prescriptions were rated as potentially inappropriate and 21.5% were changed following the pharmacist's recommendations (203).

7.3 Summary of findings from the qualitative study

The aim of this study was firstly to reveal the determinants of GP prescribing behaviour for older adults in primary care and secondly to elicit GPs' views on the potential role for broad intervention strategies involving pharmacists and/or information technology systems in general practice. Semi-structured qualitative interviews were carried out with 16 GPs with emerging themes mapped to the TDF.

This study highlighted the complexities of behavioural determinants of prescribing for older people in primary care in Ireland and the need for additional supports to optimise prescribing for this growing cohort of patients. It also showed that GPs still view the role of pharmacists and their own relationship with pharmacists in a positive way. Participants suggested that there is scope to harness the GP-pharmacist relationship to improve patient outcomes. One approach that could enhance this relationship in a way that may lead to meaningful and sustained improvements in prescribing is AD.

The findings from the cross-sectional study, systematic review and qualitative study informed the AD educational intervention for the next phase of the thesis. The cross-sectional study sets the scene by highlighting the prevalence and type of prescribing issues among older adults in primary care. These study findings then informed the systematic review as we wanted to evaluate the most appropriate pharmacist-led intervention to improve prescribing appropriateness. Having reviewed these

interventions, the next step was to carry out a qualitative study with GPs to obtain their experience of prescribing for older people in primary care and to elicit their views on the potential role for broad intervention strategies involving pharmacists and/or information technology systems in general practice. It identified AD as an approach to optimise prescribing for older people in primary care.

7.4 Summary of findings from the mixed methods study

This study assessed the feasibility and acceptability of a pharmacist-led academic detailing intervention with a sample of practising GPs using a mixed methods approach. Qualitative focus groups were carried out with 14 GPs who participated in the AD intervention on urinary incontinence in older people. The medical records for all patients aged ≥ 65 years who were attending a participating GP with a diagnosis of urinary incontinence were retrieved and analysed using a before-after approach. The intervention was well received by GPs, who deemed it acceptable and appropriate to the context of general practice. They were also willing to participate in future AD studies. Habraken *et al.* highlighted that Belgian physicians highly rated AD visits and approximately 90% of those surveyed were willing to use this service again (70). Hartung *et al.* reported strong support and satisfaction for the AD program among participating clinicians and almost all indicated that they would continue to participate in future educational sessions (174).

There was minimal or no change in the reported prescribing outcomes of the LUTS-FORTA criteria, DBI, ACB scale and the STOPP/START V2 criteria before and after the intervention. However, these findings are of value as they can provide information on possible effect sizes which can help to determine the sample size in subsequent

larger studies. This may be particularly useful where there are no data from previous studies to inform this process. The findings can also evaluate appropriate outcome measures for future trials. It is envisaged that the publication of the mixed methods study will inform and benefit other researchers planning future definitive larger studies.

7.5 Strengths and limitations

This section provides a synopsis of the overall strengths and limitations of this thesis. The strengths and limitations of the individual studies have been previously addressed in each chapter.

The thesis was designed in a structured and systematic way to identify the most appropriate intervention to be used. The cross-sectional study in the thesis sets the scene and has multiple strengths. To the best of our knowledge that was one of the first studies that used the updated STOPP/START criteria. Data comparing the prevalence of PIP and PPOs across different European sites was also scarce. Twenty researchers with various academic disciplines from three different countries contributed to this study for example, conceiving and designing the study, carrying out statistical analysis and reviewing subsequent drafts of the manuscript. This cross-disciplinary, multi-authored and multi-institutional approach added to the credibility and reliability of the study. However, the study population is relatively small (532 participants) and may limit the generalisability and insights about prescribing nationally across three countries.

The value of the systematic review is supported by the use of an explicit research question, robust methodology that included comprehensive and exhaustive search strategies, clearly defined inclusion and exclusion criteria, the use of transparent quality appraisal tools and clear reporting of results. The five included studies were conducted in the United States, the UK and New Zealand. This facilitated a cross country comparison of each study findings. Due to the heterogeneity of the interventions and outcome measures reported a narrative synthesis was carried out. A meta-analysis would have enhanced the findings of the review. Despite updating the search in May 2017 only two additional studies were relevant to the review. This highlights the lack of high quality studies on this topic.

The qualitative study obtained rich data on the challenges that GPs face when prescribing for older people in primary care in Ireland. It also informed the intervention for the mixed methods study. The framework method facilitated a systematic approach to data analysis. However, this method is more time consuming compared to the other approaches of qualitative analysis.

Triangulating the data from the qualitative focus groups and quantitative measures of prescribing allowed a richer analysis of the findings. It also afforded an opportunity to gain a more complete insight into the research topic (204). I had previously carried out qualitative work (Chapter 5) with most of the GPs who participated in the feasibility study and as a result, this helped to develop a professional relationship between us. The GPs may have been less resistant to participating in the intervention as they were familiar with the detailer who was delivering it. Attending the two day academic detailing training workshop in Boston in 2016 added rigour and consistency

to the educational approach. Permission was granted by the Alosa Foundation to use their educational materials for this study. This highlights the transferability of AD data across countries with different health systems and supports future sustainability and practicability of AD interventions. The high quality of the materials were acknowledged by the GPs in the qualitative focus groups. This study was carried out with a sample of GPs in a region of Ireland, however it remains to be seen if the potential benefits of the intervention will be observed in other geographical areas or in a larger population.

7.6 Policy implications

In 2004, the WHO commissioned a report *“Knowledge for Better Health, Strengthening Health Systems”*. This report recommended incorporating high quality research into the policy making process as a key approach to optimising international health systems (205).

I believe that the analysis of PIP and PPOs among older adults in Chapter 3 is important and that the between country comparisons may provide insight on important differences about the effect of guidelines and incentives at national level that could inform policy. Another factor that could optimise the uptake of this research into policy is the publication of the systematic review. This source of evidence has been suggested as a useful tool in policy development (206). During the focus groups of the mixed methods study, participants were asked how the AD intervention could be rolled out to GPs nationwide. Some participants highlighted that one way of communicating this research to a wider group of GPs in Ireland would

be to publish an article on the study in the GP magazine Forum. The Forum magazine is published by the ICGP.

“It might be interesting if you wrote into FORUM, that’s our GP magazine... they can do the middle page where the educational updates every month, write into that.” (GP11 Focus group 4).

In October 2016 I emailed the editor of the journal about submitting an article on the feasibility study. The editor suggested a short communication on the study, which was submitted a month later and was published in the January 2017 issue of the magazine. The publication of the short communication was a first step towards communicating my research for policy. This short communication is available in Appendix V.

Finally, I have also disseminated the research from my PhD at various national and international conferences (See Appendix VII). The use of social media especially Twitter can play an important role as a communication channel to an audience that is interested in my research. This could lead to increased collaborations with other academics outside my usual networks and communication with other healthcare professionals (207).

7.7 Future research

The next step of the feasibility study is to move to a large scale evaluation of the intervention. The overall impression from the study is that this educational service is feasible and acceptable to GPs. Up-scaling the intervention to a large scale randomised control trial would allow an assessment of its effectiveness. In order to increase the acceptability of any future interventions it would be important to

collaborate with the ICGP. Participants from the focus groups highlighted that if a future intervention was affiliated with this professional body it would optimise its approval among GPs.

“that gives a bit of an imprimatur and it ... gets people more receptive to it.”
(GP14 Focus group 5).

Another option would be an affiliation with a university body for example, the School of Pharmacy or Medicine e.g. the Department of General Practice in UCC. This would formalise the intervention and the relevant institution could become a “centre of excellence” for academic detailing in Ireland. The literature has also highlighted the importance of establishing credibility through a respected organisational identity (68). It might also be worthwhile attending CME meetings for GPs or the annual ICGP conference. A brief presentation could be given to attendees on the case for AD. It would also provide an opportunity to answer any questions relating to this educational technique. Linking academic detailing to CME credits may incentivise GPs to participate in future studies. Topic selection and educational material development should involve GPs to ensure relevance to general practice. Interventions that are tailored to participants can be powerful predictors of effectiveness (197, 208). This study involved a single visit to GPs, however, when AD interventions are sustained over time, participants have an opportunity to develop a relationship with the detailer. Regular, repeated visits would allow the detailer to understand individual participant and practice needs and provide educational and organisational support accordingly. This may result in different findings and should be further explored in future studies (209). AD studies with other healthcare

professionals such as hospital doctors and nurses should be considered. Finally, future efforts evaluating the economic benefits of AD should also be explored.

7.8 Conclusion

This thesis presents a comprehensive and detailed body of research exploring the role of the pharmacist in optimising prescribing for older people in primary care. The range of methodological approaches used, combined with a multidisciplinary, collaborative team effort throughout adds to the reliability and rigour of the thesis. The prevalence study highlighted that PIP and PPOs are prevalent among a sample of community-dwelling older people enrolled to a clinical trial in three European countries. The systematic review demonstrated that pharmacist-led interventions may improve prescribing appropriateness in community-dwelling older adults. However, the quality of evidence is low. While the qualitative study highlighted the complexities of behavioural determinants of prescribing for older people in primary care and the need for additional supports to optimise prescribing for this growing cohort of patients. At the end of this series of studies, a pharmacist-led AD intervention with GPs was identified as being potentially useful for improving prescribing behaviour. The results of the research indicate that this intervention was relevant and practical to general practice in Ireland. The evidence-based approach of AD was also highly valued by the participating GPs in the study. Going forward, AD should be up-scaled to large intervention studies and include a wider number of healthcare providers i.e. hospital doctors, dentists, nurses to assess its effectiveness. AD, which offers a pragmatic approach that can potentially optimise prescribing

practices, prevent adverse effects and improve patient health outcomes, is worthy of further investigation in an Irish context.

References

1. Gallagher P, Barry P, O'Mahony D. Inappropriate prescribing in the elderly. *J Clin Pharm Ther.* 2007;32(2):113-21.
2. OECD. Share of the population aged 65 and over, 1960 to 2011. OECD Publishing. 2011.
3. OECD. Demographic trends. OECD Publishing. 2016.
4. Office CS. Population and Labour Force Projections 2016-2046 Dublin, Government of Ireland. 2013.
5. Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol.* 2004;57(1):6-14.
6. Mallet L, Spinewine A, Huang A. The challenge of managing drug interactions in elderly people. *Lancet.* 2007;370(9582):185-91.
7. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev.* 2011;10(4):430-9.
8. Fulton MM, Allen ER. Polypharmacy in the elderly: a literature review. *J Am Acad Nurse Pract.* 2005;17(4):123-32.
9. O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. *Drugs and Aging.* 2012;29(6):437-52.
10. Boyd CM, Fortin M. Future of multimorbidity research: How should understanding of multimorbidity inform health system design? *Public Health Reviews.* 2011;33(2):451-74.

11. Mercer SW, Smith SM, Wyke S, O'Dowd T, Watt GC. Multimorbidity in primary care: developing the research agenda. *Family Practice*. 2009;26(2):79-80.
12. Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *Journal of the American Medical Association*. 2005;294(6):716-24.
13. Valderas JM, Starfield B, Sibbald B, Salisbury C, Roland M. Defining comorbidity: implications for understanding health and health services. *The Annals of Family Medicine*. 2009;7(4):357-63.
14. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. *Ann Fam Med*. 2005;3(3):223-8.
15. Boyd CM, Fortin M. Future of multimorbidity research: how should understanding of multimorbidity inform health system design. *Public Health Reviews*. 2010;32(2):451-74.
16. 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*. 2011;171(11):1013-9.
17. Jano E, Aparasu RR. Healthcare outcomes associated with Beers' criteria: a systematic review. *Annals of Pharmacotherapy*. 2007;41(3):438-48.
18. 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? *The Lancet*. 2007;370(9582):173-84.

19. Beers MH, Ouslander JG, Rollinger I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Arch Intern Med.* 1991;151(9):1825-32.
20. 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. *Br J Clin Pharmacol.* 2010;69(5):543-52.
21. Bradley MC, Motterlini N, Padmanabhan S, Cahir C, Williams T, Fahey T, et al. Potentially inappropriate prescribing among older people in the United Kingdom. *BMC Geriatr.* 2014;14:72.
22. Goulding MR. Inappropriate medication prescribing for elderly ambulatory care patients. *Arch Intern Med.* 2004;164(3):305-12.
23. Curtis LH, Ostbye T, Sendersky V, Hutchison S, Dans PE, Wright A, et al. Inappropriate prescribing for elderly Americans in a large outpatient population. *Arch Intern Med.* 2004;164(15):1621-5.
24. 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. *Am J Med.* 2004;116(6):394-401.
25. Pitkala KH, Strandberg TE, Tilvis RS. Inappropriate drug prescribing in home-dwelling, elderly patients: a population-based survey. *Arch Intern Med.* 2002;162(15):1707-12.
26. 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.* 2005;293(11):1348-58.

27. 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. *Br J Clin Pharmacol*. 2005;60(2):137-44.
28. O' Mahony D, Gallagher PF. Inappropriate prescribing in the older population: need for new criteria. *Age Ageing*. 2008;37(2):138-41.
29. Konrat C, Boutron I, Trinquart L, Auleley G-R, Ricordeau P, Ravaud P. Underrepresentation of elderly people in randomised controlled trials. The example of trials of 4 widely prescribed drugs. *PLoS One*. 2012;7(3):e33559.
30. Starfield B. Threads and yarns: weaving the tapestry of comorbidity. *Ann Fam Med*. 2006;4(2):101-3.
31. Jadad AR, To MJ, Emara M, Jones J. Consideration of multiple chronic diseases in randomized controlled trials. *JAMA*. 2011;306(24):2670-2.
32. Samsa GP, Hanlon JT, Schmader KE, Weinberger M, Clipp EC, Uttech KM, et al. A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. *J Clin Epidemiol*. 1994;47(8):891-6.
33. Marriott J, Stehlik P. A critical analysis of the methods used to develop explicit clinical criteria for use in older people. *Age Ageing*. 2012;41(4):441-50.
34. Hanlon JT, Artz MB, Pieper CF, Lindblad CI, Sloane RJ, Ruby CM, et al. Inappropriate medication use among frail elderly inpatients. *Ann Pharmacother*. 2004;38(1):9-14.
35. Bulloch MN, Olin JL. Instruments for evaluating medication use and prescribing in older adults. *J Am Pharm Assoc* 2003. 2014;54(5):530-7.

36. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc.* 2015;63(11):2227-46.
37. 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(6):936-47.
38. 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 and Ageing.* 2008;37(6):673-9.
39. Barry PJ, Gallagher P, Ryan C, O'Mahony D. START (screening tool to alert doctors to the right treatment)--an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age Ageing.* 2007;36(6):632-8.
40. 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.
41. 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.
42. Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: a French consensus panel list. *Eur J Clin Pharmacol.* 2007;63(8):725-31.
43. Naugler CT, Brymer C, Stolee P, Arcese ZA. Development and validation of an improving prescribing in the elderly tool. *Can J Clin Pharmacol.* 2000;7(2):103-7.
44. Rognstad S, Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J. The Norwegian General Practice (NORGEPRAC) criteria for assessing potentially inappropriate

prescriptions to elderly patients. A modified Delphi study. *Scand J Prim Health Care*. 2009;27(3):153-9.

45. Holt S, Schmiedl S, Thurmann PA. Potentially inappropriate medications in the elderly: the PRISCUS list. *Dtsch Arztebl Int*. 2010;107(31-32):543-51.

46. Winit-Watjana W, Sakulrat P, Kespichayawattana J. Criteria for high-risk medication use in Thai older patients. *Arch Gerontol Geriatr*. 2008;47(1):35-51.

47. McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *CMAJ*. 1997;156(3):385-91.

48. 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*. 2001;286(22):2823-9.

49. Oelke M, Becher K, Castro-Diaz D, Chartier-Kastler E, Kirby M, Wagg A, et al. Appropriateness of oral drugs for long-term treatment of lower urinary tract symptoms in older persons: results of a systematic literature review and international consensus validation process (LUTS-FORTA 2014). *Age Ageing*. 2015;44(5):745-55.

50. Hilmer SN, Mager DE, Simonsick EM, Cao Y, Ling SM, Windham BG, et al. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med*. 2007;167(8):781-7.

51. Kouladjian L, Gnjdjic D, Chen TF, Mangoni AA, Hilmer SN. Drug Burden Index in older adults: theoretical and practical issues. *Clinical interventions in aging*. 2014;9:1503.

52. Gnjdic D, Le Couteur DG, Abernethy DR, Hilmer SN. Drug burden index and Beers' criteria: impact on functional outcomes in older people living in self-care retirement villages. *J Clin Pharmacol*. 2012;52(2):258-65.
53. Tune LE. Anticholinergic effects of medication in elderly patients. *J Clin Psychiatry*. 2001;62 Suppl 21:11-4.
54. Cai X, Campbell N, Khan B, Callahan C, Boustani M. Long-term anticholinergic use and the aging brain. *Alzheimers Dement*. 2013;9(4):377-85.
55. Carriere I, Fourrier-Reglat A, Dartigues JF, Rouaud O, Pasquier F, Ritchie K, et al. Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population: the 3-city study. *Arch Intern Med*. 2009;169(14):1317-24.
56. Boustani M, Campbell N, Munger S, Maidment I, Fox C. Impact of anticholinergics on the aging brain: a review and practical application. *Aging Health*. 2008;4(3).
57. Galvin R, Moriarty F, Cousins G, Cahir C, Motterlini N, Bradley M, et al. Prevalence of potentially inappropriate prescribing and prescribing omissions in older Irish adults: findings from The Irish Longitudinal Study on Ageing study (TILDA). *Eur J Clin Pharmacol*. 2014;70(5):599-606.
58. Dimitrow MS, Airaksinen MS, Kivela SL, Lyles A, Leikola SN. Comparison of prescribing criteria to evaluate the appropriateness of drug treatment in individuals aged 65 and older: a systematic review. *J Am Geriatr Soc*. 2011;59(8):1521-30.
59. Riordan DO, Walsh KA, Galvin R, Sinnott C, Kearney PM, Byrne S. The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: A systematic review. *SAGE Open Medicine*. 2016;4:1-18.

60. Clyne B, Fitzgerald C, Quinlan A, Hardy C, Galvin R, Fahey T, et al. Interventions to Address Potentially Inappropriate Prescribing in Community-Dwelling Older Adults: A Systematic Review of Randomized Controlled Trials. *J Am Geriatr Soc*. 2016;64(6):1210-22.
61. Blenkinsopp A, Bond C, Raynor DK. Medication reviews. *Br J Clin Pharmacol*. 2012;74(4):573-80.
62. Lenaghan E, Holland R, Brooks A. Home-based medication review in a high risk elderly population in primary care--the POLYMED randomised controlled trial. *Age Ageing*. 2007;36(3):292-7.
63. 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. *Am J Med*. 1996;100(4):428-37.
64. Pearson SA, Moxey A, Robertson J, Hains I, Williamson M, Reeve J, et al. Do computerised clinical decision support systems for prescribing change practice? A systematic review of the literature (1990-2007). *BMC Health Services Research*. 2009;9:154.
65. Musen MA, Shahar Y, Shortliffe EH. Clinical Decision-Support Systems. In: Shortliffe EH, Cimino JJ, editors. *Biomedical Informatics: Computer Applications in Health Care and Biomedicine*. New York, NY: Springer New York; 2006. p. 698-736.
66. 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 and Aging*. 2013;30(1):39-49.

67. Rodondi N. OPTimising thERapy to Prevent Avoidable Hospital Admissions in the Multimorbid Older People. ClinicalTrials.gov2017. p. NCT02986425.
68. Soumerai SB, Avorn J. Principles of educational outreach ('academic detailing') to improve clinical decision making. JAMA. 1990;263(4):549-56.
69. O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, et al. Educational outreach visits: effects on professional practice and health care outcomes. Cochrane Database Syst Rev. 2007(4):CD000409.
70. Habraken H, Janssens I, Soenen K, van Driel M, Lannoy J, Bogaert M. Pilot study on the feasibility and acceptability of academic detailing in general practice. Eur J Clin Pharmacol. 2003;59(3):253-60.
71. Ilett KF, Johnson S, Greenhill G, Mullen L, Brockis J, Golledge CL, et al. Modification of general practitioner prescribing of antibiotics by use of a therapeutics adviser (academic detailer). British Journal of Clinical Pharmacology. 2000;49(2):168-73.
72. PSI. Pharmaceutical Society of Ireland, Future Pharmacy Practice in Ireland, Meeting Patients' Needs 2016:1-129.
73. Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. BMC Med Res Methodol. 2006;6:54.
74. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. J Am Geriatr Soc. 2014;62(12):2261-72.
75. Fialova D, Onder G. Medication errors in elderly people: contributing factors and future perspectives. Br J Clin Pharmacol. 2009;67(6):641-5.

76. 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. *Int J Clin Pharmacol Ther*. 2008;46(2):72-83.
77. 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. *Eur J Clin Pharmacol*. 2011;67(11):1175-88.
78. Hill-Taylor B, Walsh KA, Stewart S, Hayden J, Byrne S, Sketris IS. Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies. *J Clin Pharm Ther*. 2016;41(2):158-69.
79. Stott DJ, Gussekloo J, Kearney PM, Rodondi N, Westendorp RG, Mooijaart S, et al. Study protocol; Thyroid hormone Replacement for Untreated older adults with Subclinical hypothyroidism - a randomised placebo controlled Trial (TRUST). *BMC Endocr Disord*. 2017;17(1):6.
80. Stott DJ, Rodondi N, Kearney PM, Ford I, Westendorp RGJ, Mooijaart SP, et al. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. *New England Journal of Medicine*. 2017;0(0):1-11.
81. Viktil KK, Blix HS, Moger TA, Reikvam A. Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *Br J Clin Pharmacol*. 2007;63(2):187-95.
82. von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624):806-8.

83. Hill-Taylor B, Sketris I, Hayden J, Byrne S, O'Sullivan D, Christie R. Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. *J Clin Pharm Ther*. 2013;38(5):360-72.

84. Blanco-Reina E, Garcia-Merino MR, Ocana-Riola R, Aguilar-Cano L, Valdellos J, Bellido-Estevez I, et al. Assessing Potentially Inappropriate Prescribing in Community-Dwelling Older Patients Using the Updated Version of STOPP-START Criteria: A Comparison of Profiles and Prevalences with Respect to the Original Version. *PLoS One*. 2016;11(12):1-10.

85. Bahat G, Bay I, Tufan A, Tufan F, Kilic C, Karan MA. Prevalence of potentially inappropriate prescribing among older adults: A comparison of the Beers 2012 and Screening Tool of Older Person's Prescriptions criteria version 2. *Geriatr Gerontol Int*. 2016;1-7.

86. Hudhra K, Beci E, Petrela E, Xhafaj D, Garcia-Caballos M, Bueno-Cavanillas A. Prevalence and factors associated with potentially inappropriate prescriptions among older patients at hospital discharge. *J Eval Clin Pract*. 2016;22(5):707-13.

87. Getachew H, Bhagavathula AS, Abebe TB, Belachew SA. Inappropriate prescribing of antithrombotic therapy in Ethiopian elderly population using updated 2015 STOPP/START criteria: a cross-sectional study. *Clin Interv Aging*. 2016;11:819-27.

88. Moriarty F, Hardy C, Bennett K, Smith SM, Fahey T. Trends and interaction of polypharmacy and potentially inappropriate prescribing in primary care over 15 years in Ireland: a repeated cross-sectional study. *BMJ Open*. 2015;5(9):1-7.
89. Health Service Executive Primary Care Reimbursement Service Statistical Analysis of Claims and Payments 2014 [Internet]. 2014.
90. Teljeur C, Tyrrell E, Kelly A, O'Dowd T, Thomas S. Getting a handle on the general practice workforce in Ireland. *Ir J Med Sci*. 2014;183(2):207-13.
91. Grol R, Wensing M, Mainz J, Jung HP, Ferreira P, Hearnshaw H, et al. Patients in Europe evaluate general practice care: an international comparison. *The British Journal of General Practice*. 2000;50(460):882-7.
92. Sinnott C, Mc Hugh S, Browne J, Bradley C. GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. *BMJ Open*. 2013;3(9):1-11.
93. 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.
94. Bradley MC, Fahey T, Cahir C, Bennett K, O'Reilly D, Parsons C, et al. Potentially inappropriate prescribing and cost outcomes for older people: a cross-sectional study using the Northern Ireland Enhanced Prescribing Database. *Eur J Clin Pharmacol*. 2012;68(10):1425-33.
95. Huntley AL, Johnson R, Purdy S, Valderas JM, Salisbury C. Measures of multimorbidity and morbidity burden for use in primary care and community settings: a systematic review and guide. *The Annals of Family Medicine*. 2012;10(2):134-41.

96. Brilleman SL, Salisbury C. Comparing measures of multimorbidity to predict outcomes in primary care: a cross sectional study. *Family practice*. 2013;30(2):172-8.
97. Tinetti ME, Bogardus ST, Jr., Agostini JV. Potential pitfalls of disease-specific guidelines for patients with multiple conditions. *N Engl J Med*. 2004;351(27):2870-4.
98. O'Sullivan D, O'Mahony D, O'Connor MN, Gallagher P, Gallagher J, Cullinan S, et al. Prevention of Adverse Drug Reactions in Hospitalised Older Patients Using a Software-Supported Structured Pharmacist Intervention: A Cluster Randomised Controlled Trial. *Drugs & Aging*. 2016;33(1):63-73.
99. Caskie GI, Willis SL. Congruence of self-reported medications with pharmacy prescription records in low-income older adults. *Gerontologist*. 2004;44(2):176-85.
100. Anrys P, Boland B, Degryse JM, De Lepeleire J, Petrovic M, Marien S, et al. STOPP/START version 2-development of software applications: easier said than done? *Age Ageing*. 2016;45(5):589-92.
101. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet*. 2007;370(9582):173-84.
102. O'Sullivan D, Byrne S, O'Mahony D. An evaluation of the inappropriate prescribing in older residents in long term care facilities in the greater Cork and Northern Ireland regions using the STOP and Beers' criteria. Centre for Ageing Research and Development in Ireland (CARDI). 2011.
103. 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.

104. Bradley MC, Fahey T, Cahir C, Bennett K, O'Reilly D, Parsons C, et al. Potentially inappropriate prescribing and cost outcomes for older people: a cross-sectional study using the Northern Ireland Enhanced Prescribing Database. *Eur J Clin Pharmacol.* 2012;68(10):1425-33.
105. Bradley MC, Motterlini N, Padmanabhan S, Cahir C, Williams T, Fahey T, et al. Potentially inappropriate prescribing among older people in the United Kingdom. *BMC Geriatrics.* 2014;14(1):72.
106. Curtis LH, Ostbye T, Sendersky V, Hutchison S, Dans PE, Wright A, et al. Inappropriate prescribing for elderly Americans in a large outpatient population. *Arch Intern Med.* 2004;164(15):1621-5.
107. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet.* 2007;370(9582):173-84.
108. 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.* 2009;68(6):936-47.
109. Hanlon JT, Schmader KE. The medication appropriateness index at 20: where it started, where it has been, and where it may be going. *Drugs Aging.* 2013;30(11):893-900.
110. Hanlon JT, Artz MB, Pieper CF, Lindblad CI, Sloane RJ, Ruby CM, et al. Inappropriate medication use among frail elderly inpatients. *Annals of Pharmacotherapy.* 2004;38(1):9-14.
111. Muijers PE, Kottnerus JA, Sijbrandij J, Janknegt R, Grol RP. Changing relationships: attitudes and opinions of general practitioners and pharmacists

regarding the role of the community pharmacist. *Pharmacy World and Science*. 2003;25(5):235-41.

112. Patterson SM, Cadogan CA, Kerse N, Cardwell CR, Bradley MC, Ryan C, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database of Systematic Reviews* 2014(10):1-119.

113. Castelino RL, Bajorek BV, Chen TF. Targeting Suboptimal Prescribing in the Elderly: A Review of the Impact of Pharmacy Services. *Annals of Pharmacotherapy*. 2009;43(6):1096-106.

114. Alldred DP, Kennedy MC, Hughes C, Chen TF, Miller P. Interventions to optimise prescribing for older people in care homes. *Cochrane Database Syst Rev*. 2016;2:CD009095.

115. Walsh KA, O'Riordan D, Kearney PM, Timmons S, Byrne S. Improving the appropriateness of prescribing in older patients: a systematic review and meta-analysis of pharmacists' interventions in secondary care. *Age and Ageing*. 2016;45(2):201-9.

116. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine* 2009;151(4):264-9, .

117. Shade MY, Berger AM, Chaperon C. Potentially Inappropriate Medications in Community-Dwelling Older Adults. *Research in Gerontological Nursing*. 2014;7(4):178-92.

118. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *British Medical Journal BMJ*. 2011;343:1-9.

119. Collaboration. C. Suggested risk of bias criteria for EPOC reviews.
<http://epoccochraneorg/resources/epoc-resources-review-authors.1-4>.
120. Bryant LJM, Coster G, Gamble GD, McCormick RN. The General Practitioner-Pharmacist Collaboration (GPPC) study: a randomised controlled trial of clinical medication reviews in community pharmacy. *The International Journal of Pharmacy Practice*. 2011;19(2):94-105.
121. 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.
122. Taylor CT, Byrd DC, Krueger K. Improving primary care in rural Alabama with a pharmacy initiative. *American Journal of Health-System Pharmacy*. 2003;60(11):1123-9.
123. Richmond S, Morton V, Cross B, Wong ICK, Russell I, Philips Z, et al. Effectiveness of shared pharmaceutical care for older patients: RESPECT trial findings. *British Journal of General Practice*. 2010;60(570):10-9.
124. Raebel MA, Charles J, Dugan J, Carroll NM, Korner EJ, Brand DW, et al. Randomized trial to improve prescribing safety in ambulatory elderly patients. *J Am Geriatr Soc*. 2007;55(7):977-85.
125. 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. *Arch Intern Med*. 2003;163(22):2716-24.
126. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Arch Intern Med*. 1997;157(14):1531-6.

127. 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*. 2001;286(22):2823-9.
128. Schmader KE, Hanlon JT, Landsman PB, Samsa GP, Lewis IK, Weinberger M. Inappropriate prescribing and health outcomes in elderly veteran outpatients. *Ann Pharmacother*. 1997;31(5):529-33.
129. Lund BC, Carnahan RM, Egge JA, Chrischilles EA, Kaboli PJ. Inappropriate prescribing predicts adverse drug events in older adults. *Ann Pharmacother*. 2010;44(6):957-63.
130. Hanlon JT, Sloane RJ, Pieper CF, Schmader KE. Association of adverse drug reactions with drug-drug and drug-disease interactions in frail older outpatients. *Age Ageing*. 2011;40(2):274-7.
131. Kaur S, Mitchell G, Vitetta L, Roberts MS. Interventions that can Reduce Inappropriate Prescribing in the Elderly A Systematic Review. *Drugs & Aging*. 2009;26(12):1013-28.
132. Topinkova E, Baeyens JP, Michel JP, Lang PO. Evidence-based strategies for the optimization of pharmacotherapy in older people. *Drugs & Aging*. 2012;29(6):477-94.
133. Avery AJ, Rodgers S, Cantrill JA, Armstrong S, Cresswell K, Eden M, et al. A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis. *Lancet*. 2012;379(9823):1310-9.

134. Hartung DM, Hamer A, Middleton L, Haxby D, Fagnan LJ. A pilot study evaluating alternative approaches of academic detailing in rural family practice clinics. *BMC Fam Pract.* 2012;13:129.
135. Maltais R, Schmidt T, Chhina H, Mazowita G, Marra C, Tugwell P, et al. Academic detailing to optimize care for RA by family physicians-results of a satisfaction survey. *Journal of Rheumatology.* 2014;41(7):1494-5.
136. Van Hoof TJ HL, Miller NE, Pappas MS, Fischer MA. Characteristics of Academic Detailing results from a systematic review. *American Health & Drug Benefits.* 2015;8(8):414-42.
137. Lowrie R, Lloyd SM, McConnachie A, Morrison J. A cluster randomised controlled trial of a pharmacist-led collaborative intervention to improve statin prescribing and attainment of cholesterol targets in primary care. *PLoS One.* 2014;9(11):e113370.
138. Cowper PA, Weinberger M, Hanlon JT, Landsman PB, Samsa GP, Uttech KM, et al. The cost-effectiveness of a clinical pharmacist intervention among elderly outpatients. *Pharmacotherapy.* 1998;18(2):327-32.
139. Milton JC, Hill-Smith I, Jackson SH. Prescribing for older people. *British Medical Journal.* 2008;7644:606.
140. 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.* 2011;171(11):1013-9.
141. Jano E, Aparasu RR. Healthcare outcomes associated with Beers' criteria: a systematic review. *Ann Pharmacother.* 2007;41(3):438-47.

142. 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.
143. Eccles MP, Armstrong D, Baker R, Cleary K, Davies H, Davies S, et al. An implementation research agenda. *Implementation Science*. 2009;4(18):1-7.
144. Barber N. What constitutes good prescribing? *British Medical Journal* 1995;310(6984):923-5.
145. Inman W, Pearce G. Prescriber profile and post-marketing surveillance. *The Lancet*. 342(8872):658-61.
146. Feely J, Chan R, McManus J, O'Shea B. The influence of hospital-based prescribers on prescribing in general practice. *Pharmacoeconomics*. 1999;16(2):175-81.
147. Peay MY, Peay ER. The role of commercial sources in the adoption of a new drug. *Social Science and Medicine*. 1988;26(12):1183-9.
148. Eccles M, Grimshaw J, Walker A, Johnston M, Pitts N. Changing the behavior of healthcare professionals: the use of theory in promoting the uptake of research findings. *Journal of Clinical Epidemiology*. 2005;58.
149. 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.
150. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implementation Science*. 2012;7(1):37.

151. 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*. 2015;79(5):860-9.
152. Ritchie J, Lewis J, Nicholls CM, Ormston R. *Qualitative research practice: A guide for social science students and researchers*: Sage; 2013.
153. 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 and Health*. 2010;25(10):1229-45.
154. 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. *British Medical Journal Open*. 2014;4(12):1-18.
155. Anthierens S, Tansens A, Petrovic M, Christiaens T. Qualitative insights into general practitioners views on polypharmacy. *BMC Family Practice*. 2010;11(1):1.
156. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007;19(6):349-57.
157. Adams WL, McIlvain HE, Lacy NL, Magsi H, Crabtree BF, Yenny SK, et al. Primary care for elderly people: why do doctors find it so hard? *Gerontologist*. 2002;42(6):835-42.
158. Braddock CH, 3rd, Snyder L. The doctor will see you shortly. The ethical significance of time for the patient-physician relationship. *Journal of General Internal Medicine*. 2005;20(11):1057-62.

159. Bradley F. What key components are required to improve pharmacist-GP collaboration? *Pharmaceutical Journal*. 2012;289(7733):608.
160. 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.
161. Castillo RS, Kelemen A. Considerations for a successful clinical decision support system. *Computers, Informatics, Nursing*. 2013;31(7):319-28.
162. Jin M, Naumann T, Regier L, Bugden S, Allen M, Salach L, et al. A brief overview of academic detailing in Canada: Another role for pharmacists. *Canadian Pharmacists Journal*. 2012;145(3):142-6.
163. Avorn J, Soumerai SB. Improving drug-therapy decisions through educational outreach. A randomized controlled trial of academically based "detailing". *N Engl J Med*. 1983;308(24):1457-63.
164. 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*. 2012;7(86):1-13.
165. Birt L, Scott S, Cavers D, Campbell C, Walter F. Member Checking: A Tool to Enhance Trustworthiness or Merely a Nod to Validation? *Qualitative Health Research*. 2016:1-10.
166. Sansom A, Calitri R, Carter M, Campbell J. Understanding quit decisions in primary care: a qualitative study of older GPs. *BMJ Open*. 2016;6(2):e010592.

167. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn*. 2002;21(2):167-78.
168. Hunskaar S, Lose G, Sykes D, Voss S. The prevalence of urinary incontinence in women in four European countries. *BJU Int*. 2004;93(3):324-30.
169. Bartoli S, Aguzzi G, Tarricone R. Impact on quality of life of urinary incontinence and overactive bladder: a systematic literature review. *Urology*. 2010;75(3):491-500.
170. Hunskaar S, Arnold EP, Burgio K, Diokno AC, Herzog AR, Mallett VT. Epidemiology and natural history of urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct*. 2000;11(5):301-19.
171. Norton P, Brubaker L. Urinary incontinence in women. *Lancet*. 2006;367(9504):57-67.
172. Corcos J, Beaulieu S, Donovan J, Naughton M, Gotoh M. Quality of life assessment in men and women with urinary incontinence. *J Urol*. 2002;168(3):896-905.
173. Levy R, Muller N. Urinary incontinence: economic burden and new choices in pharmaceutical treatment. *Advances in therapy*. 2006;23(4):556-73.
174. Hartung DM, Hamer A, Middleton L, Haxby D, Fagnan LJ. A pilot study evaluating alternative approaches of academic detailing in rural family practice clinics. *BMC Fam Pract*. 2012;13:129.

175. Maltais R, Schmidt T, Chhina H, Mazowita G, Marra C, Tugwell P, et al., editors. Academic Detailing to Optimize Care for RA by Family Physicians-Results of a Satisfaction Survey. *Journal of Rheumatology*; 2014, 41 (7):1494-95
176. Frich JC, Hoyer S, Lindbaek M, Straand J. General practitioners and tutors' experiences with peer group academic detailing: a qualitative study. *BMC Fam Pract*. 2010;11:12.
177. Clyne B, Smith SM, Hughes CM, Boland F, Bradley MC, Cooper JA, et al. Effectiveness of a Multifaceted Intervention for Potentially Inappropriate Prescribing in Older Patients in Primary Care: A Cluster-Randomized Controlled Trial (OPTI-SCRIPT Study). *Ann Fam Med*. 2015;13(6):545-53.
178. Clyne B, Cooper JA, Hughes CM, Fahey T, Smith SM, Team O-SS. A process evaluation of a cluster randomised trial to reduce potentially inappropriate prescribing in older people in primary care (OPTI-SCRIPT study). *Trials*. 2016;17(386):1-15.
179. Creswell JW, Plano Clark VL. *Designing and Conducting Mixed Methods Research*. Sage. 2011.
180. Eldridge SM, Lancaster GA, Campbell MJ, Thabane L, Hopewell S, Coleman CL, et al. Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework. *PLoS One*. 2016;11(3):e0150205.
181. Arain M, Campbell MJ, Cooper CL, Lancaster GA. What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC medical research methodology*. 2010;10(1):67.
182. Bazeley P. Integrating Data Analyses in Mixed Methods Research. *Journal of Mixed Methods Research*. 2009;3(3):203-7.

183. Woolley CM. Meeting the Mixed Methods Challenge of Integration in a Sociological Study of Structure and Agency. *Journal of Mixed Methods Research*. 2009;3(1):7-25.
184. Health A. <http://alosahealth.org/>. Accessed March 2016.
185. NVivo qualitative data analysis Software; QSR International Pty Ltd. Version 10.22
186. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative Research in Psychology*. 2006;3(2):77-101.
187. Duran CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. *Eur J Clin Pharmacol*. 2013;69(7):1485-96.
188. Ailabouni N, Mangin D, Nishtala PS. Deprescribing anticholinergic and sedative medicines: protocol for a Feasibility Trial (DEFEAT-polypharmacy) in residential aged care facilities. *BMJ Open*. 2017;7(4):e013800.
189. Health Products Regulatory Authority (HPRA) SPC Database. www.hpra.ie.
190. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. *J Psychiatr Res*. 2011;45(5):626-9.
191. Teare MD, Dimairo M, Shephard N, Hayman A, Whitehead A, Walters SJ. Sample size requirements to estimate key design parameters from external pilot randomised controlled trials: a simulation study. *Trials*. 2014;15:264.
192. Bugge C, Williams B, Hagen S, Logan J, Glazener C, Pringle S, et al. A process for Decision-making after Pilot and feasibility Trials (ADePT): development following a feasibility study of a complex intervention for pelvic organ prolapse. *Trials*. 2013;14:353.

193. Cameron RA DT, Richardson S, Ahmed E, Sukumaran A. . Lessons from the field: Applying the Good Reporting of A Mixed Methods Study (GRAMMS) framework'. *Electronic Journal of Business Research Methods*. 2013;11(2):53-64.
194. O'Cathain A, Murphy E, Nicholl J. The quality of mixed methods studies in health services research. *J Health Serv Res Policy*. 2008;13(2):92-8.
195. Allen M, Ferrier S, O'Connor N, Fleming I. Family physicians' perceptions of academic detailing: a quantitative and qualitative study. *BMC Med Educ*. 2007;7:36.
196. van Eijk ME, Avorn J, Porsius AJ, de Boer A. Reducing prescribing of highly anticholinergic antidepressants for elderly people: randomised trial of group versus individual academic detailing. *BMJ*. 2001;322(7287):654-7.
197. Figueiras A, Sastre I, Tato F, Rodriguez C, Lado E, Caamano F, et al. One-to-one versus group sessions to improve prescription in primary care: a pragmatic randomized controlled trial. *Med Care*. 2001;39(2):158-67.
198. Soumerai SB. Principles and uses of academic detailing to improve the management of psychiatric disorders. *Int J Psychiatry Med*. 1998;28(1):81-96.
199. Dreischulte T, Donnan P, Grant A, Hapca A, McCowan C, Guthrie B. Safer Prescribing--A Trial of Education, Informatics, and Financial Incentives. *N Engl J Med*. 2016;374(11):1053-64.
200. Avorn J, Soumerai SB. Improving drug-therapy decisions through educational outreach. A randomized controlled trial of academically based "detailing". *New England Journal of Medicine*. 1983;308(24):1457-63.
201. Thabane L, Hopewell S, Lancaster GA, Bond CM, Coleman CL, Campbell MJ, et al. Methods and processes for development of a CONSORT extension for reporting pilot randomized controlled trials. *Pilot Feasibility Stud*. 2016;2:25.

202. Haag JD, Davis AZ, Hoel RW, Armon JJ, Odell LJ, Dierkhising RA, et al. Impact of Pharmacist-Provided Medication Therapy Management on Healthcare Quality and Utilization in Recently Discharged Elderly Patients. *American Health and Drug Benefits*. 2016;9(5):259-67.
203. Campins L, Serra-Prat M, Gózaló I, López D, Palomera E, Agustí C, et al. Randomized controlled trial of an intervention to improve drug appropriateness in community-dwelling polymedicated elderly people. *Family Practice*. 2017;34(1):36-42.
204. Doyle L, Brady A-M, Byrne G. An overview of mixed methods research. *Journal of Research in Nursing*. 2009;14(2):175-85.
205. WHO. World report on knowledge for better health: strengthening health systems. Available from <http://www.who.int/rpc/meetings/pub1/en/> 2004. Accessed July 2017.
206. Lavis J, Davies H, Oxman A, Denis JL, Golden-Biddle K, Ferlie E. Towards systematic reviews that inform health care management and policy-making. *J Health Serv Res Policy*. 2005;10 Suppl 1:35-48.
207. Barry AR, Pearson GJ. Professional use of social media by pharmacists. *Can J Hosp Pharm*. 2015;68(1):22-7.
208. Hulscher ME, van Drenth BB, Mookink HG, van De Lisdonk EH, van Der Wouden JC, van Weel C, et al. Tailored outreach visits as a method for implementing guidelines and improving preventive care. *Int J Qual Health Care*. 1998;10(2):105-12.
209. Desveaux L, Saragosa M, Rogers J, Bevan L, Loshak H, Moser A, et al. Improving the appropriateness of antipsychotic prescribing in nursing homes: a

mixed-methods process evaluation of an academic detailing intervention. *Implement Sci.* 2017;12(1):71.

Appendix I. Supplementary material for Chapter 3.

Supplementary material 1. STOPP/START criteria version 2 applied to the TRUST dataset

Physiological system	Criteria	Criteria included	Number (%) of criteria included out of total criteria
	STOPP criteria		
Indication of medication	<p>A1. Any drug prescribed without an evidence-based clinical indication.</p> <p>A2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.</p> <p>A3. Any duplicate drug class prescription i.e. 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).</p>	<p>X</p> <p>X</p> <p>✓</p>	1/3 (33.3)
Cardiovascular system	<p>B1. Digoxin for heart failure with preserved systolic ventricular function (no clear evidence of benefit)</p> <p>B2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).</p> <p>B3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).</p> <p>B4. Beta blocker with symptomatic bradycardia (< 50/min), type II heart block or complete heart block (risk of profound hypotension, asystole).</p> <p>B5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)</p> <p>B6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).</p> <p>B7. 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).</p> <p>B8. 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).</p>	<p>X</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>X</p> <p>✓</p> <p>✓</p> <p>X</p>	7/13 (53.8)

	<p>B9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).</p> <p>B10. Centrally-acting antihypertensives (i.e. 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).</p> <p>B11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.</p> <p>B12. Aldosterone antagonists (i.e. spironolactone, eplerenone) with concurrent potassium-conserving drugs (i.e. 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).</p> <p>B13. Phosphodiesterase type-5 inhibitors (i.e. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent daily nitrate therapy for angina (risk of cardiovascular collapse).</p>	<p>✓</p> <p>X</p> <p>X</p> <p>X</p> <p>✓</p>	
Antiplatelet/Anticoagulant drugs	<p>C1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).</p> <p>C2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).</p> <p>C3. 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).</p> <p>C4. 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)</p>	<p>X</p> <p>✓</p> <p>✓</p> <p>X</p>	7/11 (63.6)
	<p>C5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation without a clear indication for aspirin (no added benefit from aspirin).</p> <p>C6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease without a clear indication for anticoagulant therapy (no added benefit from dual therapy).</p>	<p>✓</p> <p>✓</p>	

	<p>C7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).</p> <p>C8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (i.e. thrombophilia) for > 6 months, (no proven added benefit).</p> <p>C9. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (i.e. thrombophilia) for > 12 months (no proven added benefit).</p> <p>C10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of gastrointestinal bleeding).</p> <p>C11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease).</p>	<p>✓</p> <p>X</p> <p>X</p> <p>✓</p> <p>✓</p>	
CNS & Psychotropic drugs	<p>D1. Tricyclic antidepressants with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).</p> <p>D2. Initiation of tricyclic antidepressants as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).</p> <p>D3. Neuroleptics with moderate-marked antimuscarinic/anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenazine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).</p> <p>D4. 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).</p> <p>D5. 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 > 2 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).</p> <p>D6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms).</p> <p>D7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity).</p> <p>D8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).</p>	<p>✓</p> <p>X</p> <p>✓</p> <p>X</p> <p>X</p> <p>✓</p> <p>✓</p> <p>✓</p>	8/14 (57.1)

	<p>D9. 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).</p> <p>D10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).</p> <p>D11. 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).</p> <p>D12. 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).</p> <p>D13. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy).</p> <p>D14. First-generation antihistamines (safer, less toxic antihistamines now widely available).</p>	<p>X</p> <p>X</p> <p>✓</p> <p>X</p> <p>✓</p> <p>✓</p>	
Renal system	<p>E1. 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).</p> <p>E2. Direct thrombin inhibitors (i.e. dabigatran) if eGFR < 30 ml/min/1.73m² (risk of bleeding).</p> <p>E3. Factor Xa inhibitors (i.e. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m² (risk of bleeding).</p> <p>E4. NSAID's if eGFR < 50 ml/min/1.73m² (risk of deterioration in renal function).</p> <p>E5. Colchicine if eGFR < 10 ml/min/1.73m² (risk of colchicine toxicity).</p> <p>E6. Metformin if eGFR < 30 ml/min/1.73m² (risk of lactic acidosis).</p>	<p>X</p> <p>X</p> <p>X</p> <p>X</p> <p>X</p> <p>X</p>	0/6 (0)
Gastrointestinal system	<p>F1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).</p> <p>F2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).</p>	<p>✓</p> <p>X</p> <p>✓</p>	2/4 (50)

	<p>F3. Drugs likely to cause constipation (i.e. 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).</p> <p>F4. Oral elemental iron doses greater than 200 mg daily (i.e. ferrous fumarate > 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate > 1800 mg/day; no evidence of enhanced iron absorption above these doses).</p>	X	
Respiratory system	<p>G1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).</p> <p>G2. 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).</p> <p>G3. Antimuscarinic bronchodilators (i.e. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention).</p> <p>G4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).</p> <p>G5. Benzodiazepines with acute or chronic respiratory failure i.e. $pO_2 < 8.0 \text{ kPa} \pm pCO_2 > 6.5 \text{ kPa}$ (risk of exacerbation of respiratory failure).</p>	<p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>X</p>	4/5 (80)
Musculoskeletal system	<p>H1. 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).</p> <p>H2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).</p> <p>H3. 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).</p> <p>H4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis (risk of systemic corticosteroid side-effects).</p> <p>H5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).</p>	<p>✓</p> <p>✓</p> <p>X</p> <p>X</p> <p>✓</p>	6/9 (66.7)

	<p>H6. Long-term NSAID or colchicine (> 3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor i.e. allopurinol, febuxostat (xanthine-oxidase inhibitors are first choice prophylactic drugs in gout).</p> <p>H7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke).</p> <p>H8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease).</p> <p>H9. 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).</p>	<p>X</p> <p>✓</p> <p>✓</p> <p>✓</p>	
Urogenital system	<p>I1. 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).</p> <p>I2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)</p>	<p>✓</p> <p>✓</p>	2/2 (100)
Endocrine system	<p>J1. Sulphonylureas with a long duration of action (i.e. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).</p> <p>J2. Thiazolidinediones (i.e. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure).</p> <p>J3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).</p> <p>J4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).</p> <p>J5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).</p> <p>J6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of hypogonadism indication).</p>	<p>✓</p> <p>✓</p> <p>X</p> <p>✓</p> <p>✓</p> <p>✓</p>	5/6 (83.3)
Drugs that predictably increase the risk of falls in older people	<p>K1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).</p> <p>K2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).</p> <p>K3. Vasodilator drugs (i.e. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers, diazoxide, minoxidil, hydralazine) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure \geq 20mmHg (risk of syncope, falls).</p>	<p>✓</p> <p>✓</p> <p>X</p>	3/4 (75)

	K4. Hypnotic Z-drugs i.e. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).	✓	
Analgesic drugs	L1. 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).	X	2/3 (66.7)
	L2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation).	✓	
	L3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain).	✓	
Antimuscarinic/Anticholinergic drug burden	N. Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties (i.e. bladder antispasmodics, intestinal antispasmodics, tricyclic antidepressants, first generation antihistamines) (risk of increased antimuscarinic/anticholinergic toxicity).	✓	1/1 (100)
Total STOPP criteria n=80			48/80 (60)
	START criteria		
Cardiovascular system	A1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.	✓	7/8 (87.5)
	A2. 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.	✓	
	A3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.	✓	
	A4. 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.	X	
	A5. 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.	✓	
	A6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.	✓	
	A7. Beta-blocker with ischaemic heart disease.	✓	
	A8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprololorcarvedilol) with stable systolic heart failure.	✓	
Respiratory system	B1. Regular inhaled beta 2 agonist or antimuscarinic bronchodilator (i.e. ipratropium, tiotropium) for mild to moderate asthma or COPD.	✓	1/3 (33.3)

	B2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids.	X	
	B3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%).	X	
Central nervous system & Eyes	C1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability.	✓	3/6 (50)
	C2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.	X	
	C3. Acetylcholinesterase inhibitor (i.e. donepezil, rivastigmine, galantamine) for mild-moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).	✓	
	C4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.	✓	
	C5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.	X	
	C6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.	X	
Gastrointestinal system	D1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.	✓	2/2 (100)
	D2. Fibre supplements (i.e. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation.	✓	
Musculoskeletal system	E1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.	✓	7/7 (100)
	E2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.	✓	
	E3. 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).	✓	
	E4. Bone anti-resorptive or anabolic therapy (i.e. 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).	✓	
	E5. 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).	✓	
	E6. Xanthine-oxidase inhibitors (i.e. allopurinol, febuxostat) with a history of recurrent episodes of gout.	✓	

	E7. Folic acid supplement in patients taking methotexate.	✓	
Endocrine system	F1. ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. overt dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment.	X	0/1 (0)
Urogenital system	G1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary.	X	1/3 (33.3)
	G2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary.	X	
	G3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.	✓	
Analgesics	H1. 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.	X	1/2 (50)
	H2. Laxatives in patients receiving opioids regularly.	✓	
Vaccines	I1: Seasonal trivalent influenza vaccine annually.	X	0/2 (0)
	I2: Pneumococcal vaccine every 5 years, according to national guidelines	X	
Total START criteria n=34			22/34 (64.7)

Supplementary material 2. STROBE statement

Section/topic	Item no	Recommendation	Reported on page no
Title			
Title	1	(a) Indicate the study's design with a commonly used term in the title or the abstract.	38
Abstract			
Structured summary	1	(b) Provide in the abstract an informative and balanced summary of what was done and what was found.	39-40
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported.	42-43
Objectives	3	State specific objectives, including any prespecified hypotheses.	43
Methods			
Study design	4	Present key elements of study design early in the paper.	44
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.	44-48
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants.	44-48
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	44-48
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.	44-48
Bias	9	Describe any efforts to address potential sources of bias.	44-48
Study size	10	Explain how the study size was arrived at.	44-48
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.	44-48
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding.	44-48

		(b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) If applicable, describe analytical methods taking account of sampling strategy. (e) Describe any sensitivity analyses.	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study i.e. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram.	48-49
Descriptive data	14*	(a) Give characteristics of study participants (i.e. demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate number of participants with missing data for each variable of interest.	48-49
Outcome data	15*	Report numbers of outcome events or summary measures.	48-58
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (i.e., 95% confidence interval). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.	48-58
Other analyses	17	Report other analyses done—i.e. analyses of subgroups and interactions, and sensitivity analyses.	48-58
Discussion			
Key results	18	Summarise key results with reference to study objectives.	59
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	64-66
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	59-64
Generalisability	21	Discuss the generalisability (external validity) of the study results.	59-64
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.	67-68

*Give information separately for exposed and unexposed groups.

Appendix II. Supplementary material for Chapter 4.

Supplementary material 3. Table of databases and search terms applied.

Database	Search terms applied
CINAHL	AGED OR aged, 65 and over OR middle aged OR elderly AND Primary care OR primary health care OR community AND Pharmacist* AND Prescription OR prescribing
ClinicalTrials.gov	(pharmacist or pharmacists) AND (prescribing OR prescription) AND (inappropriate OR strategy OR strategies OR improving OR improve OR optimise OR optimize) AND (primary care OR primary health care OR community OR outpatient care) Adult, Senior
Cochrane Database of Systematic Reviews	"aged" or "aged, over 65" or "middle aged" or "elderly" AND prescribing or prescription or "inappropriate prescribing" AND "primary care" or "primary health care" or "outpatient care" or "community" AND pharmacist* or "pharmaceutical care" or pharmacist* intervention
Embase	'aged' OR 'aged' OR 'middle aged' OR 'middle aged' OR 'aged, over 65' OR 'elderly' OR 'elderly' AND 'primary care' OR 'primary health care' OR 'outpatient care' AND prescribing OR prescription* AND pharmacist* OR 'pharmaceutical care'
Medline (through OVID)	(prescribing or prescription) AND (aged or middle aged or elderly) AND (primary care or primary health care or elderly care or outpatient care) AND (pharmacist* or pharmaceutical care)
metaRegister of Controlled Trials (mRCT)	(pharmacist or pharmacists) AND (prescribing OR prescription) AND (inappropriate OR improving OR improve OR optimise OR optimize) AND (primary care OR primary health care OR outpatient care OR community OR general practice)
ProQuest Dissertations & Theses	(aged or elderly OR "middle aged") AND ("primary care" or "primary health care" OR community or "outpatient care") AND (prescribing or "drug prescribing" OR prescription* or "drug prescription*") AND (pharmacist* or clinical pharmacist* OR "pharmaceutical care" OR "pharmacy intervention" or "clinical intervention" OR "pharmacist intervention" or "clinical pharmacist intervention")
PubMed	((("primary care" or "primary health care" or "outpatient care")) AND ((prescribing or prescription*))) AND (("aged" or "middle aged" or elderly))) AND ((pharmacist* or "pharmaceutical care"))

Database	Search terms applied
ScienceDirect	aged OR "middle aged" OR "elderly" AND "primary care" OR "primary health care" OR community OR "outpatient care" AND prescribing OR prescription* OR "appropriate prescribing" OR "inappropriate prescribing" OR "potentially inappropriate prescribing" AND "clinical pharmacist" OR pharmacist* OR "pharmaceutical care" OR "pharmacy intervention" or "clinical intervention" OR "pharmacist intervention" or "clinical pharmacist intervention"[All Sources(Medicine and Dentistry, Nursing and Health Professions, Pharmacology, Toxicology and Pharmaceutical Science)].
Trip	"(title: aged OR middle aged OR elderly AND primary care OR primary health care OR outpatient care)(title: pharmacist* OR pharmaceutical care)(title: usual care OR control)(prescribing OR prescription)", by quality
University of York Centre for Reviews and Dissemination	(aged) OR ("middle aged") OR (elderly) AND (prescribing or prescription* or "drug prescribing" or "drug prescription*") AND ("primary care") OR ("primary health care") OR ("outpatient care") AND (pharmacist* or "clinical pharmacist*" or "pharmaceutical care" OR "pharmacist* intervention" OR "clinical pharmacist* intervention")
ISI Web of Science	("aged " or "middle aged" or elderly) Timespan=All years, Search language=Auto AND ("primary care" or "primary health care" or "outpatient care") Timespan=All years, Search language=Auto AND (prescribing or prescription*) Timespan=All years, Search language=Auto AND (pharmacist* or "pharmaceutical care") Timespan=All years, Search language=Auto

Supplementary material 4. Table of ongoing and excluded articles reviewed and reasons for exclusion

Study Number	Article	Reason for exclusion
1.	Developing Pharmacist-led Research to Educate and Sensitive Community Residents to the Inappropriate Prescription Burden in the Elderly. Source: Clinicaltrials.gov	This study is currently ongoing. Study Start Date: March 2014 Estimated Study Completion Date: September 2016
2.	Inappropriate Prescription in Elderly and Polypharmacy Patients in Primary Care. PHARM-PC Trial. Source: Clinicaltrials.gov	This study is not yet open for participant recruitment. Study Start Date: October 2014 Estimated Study Completion Date: April 2016
3.	A Pilot Study to Reduce Inappropriate Anticholinergic Prescribing in the Elderly. Source: Clinicaltrials.gov	This study is currently recruiting participants Study Start Date: September 2014 Estimated Study Completion Date: December 2015
4.	Educational Intervention to Reduce Drug-related Hospitalizations in Elderly Primary Health Care Patients.Source: Clinicaltrials.gov	Emailed author for full paper. 12/12/14 10.50am. No reply Emailed author again on 13/01/15 11.35am. No reply
5.	Minimizing Risk and Maximizing Outcomes in Geriatric Patients Through Integrated Clinical Pharmacy Services in an Innovative Model of Community Practice. Source: Clinicaltrials.gov	The recruitment status of this study is unknown because the information has not been verified recently. Observational study
6.	Study of Whether Educational Visits to Primary Care Professionals Improves the Quality of Care They Provide. Source: Clinicaltrials.gov	Not relevant. The intervention was evaluated using Prescribing Analysis and Cost (PACT) data for antidepressant drugs

7.	An Intervention Study to Reduce the Use and Impact of Potentially Inappropriate Medications Among Older Adults. Source: Clinicaltrials.gov	Emailed author for full paper 12/12/14, 11.55am. Author replied 12/12/14, 5pm with the following statement “Unfortunately our trial did not involve a pharmacist intervention so would not be relevant for your review”
8.	Pharmacist-led Medicines Management Outpatient Service Source: Clinicaltrials.gov	Emailed author for full paper 12/12/14 12.05pm. Author replied 05/01/15 with the following comment “The Medicines Management Outpatient Service research is currently in progress therefore, unfortunately it is not possible to share details at this stage”
9.	Rationalisation of Polypharmacy in the Elderly by the RASP Instrument Source: Clinicaltrials.gov	Emailed author for full paper 12/12/14 12.24pm. Author replied on 13/01/15 with following comment “I am afraid that our manuscript concerning the RASP study in hospital setting is still in the makings. We are currently finishing it as we speak. Afterwards we will normally finish a short proof-of-concept study, which was performed in primary care”
10.	Randomized Controlled Trial of Enhanced Pharmacy Care in Older Veteran Outpatients Source: Clinicaltrials.gov	Emailed author for full paper 12/12/14 12.30pm. No response Emailed author again on 13/01/15 at 11.50am. No response
11.	Preventing Falls Through Enhanced Pharmaceutical Care Source: Clinicaltrials.gov	Full article obtained. The purpose of this study was to assess the effects of a community pharmacy-based falls-prevention Program.
12.	The impact of clinical pharmacists' consultations on physicians' geriatric drug prescribing. A randomized controlled trial. Lipton, H, Bero, L, Joyce, Bird, A, McPhee, S: McPhee. <i>Medical Care</i> 1992.Vol. 30, No. 7 (Jul., 1992), pp. 646-658	Full article obtained Intervention in secondary care. Not a validated tool in 1992
13.	Elderly people still given inappropriate drugs. <i>Pharmaceutical Journal</i> . 2006. 276, 7384. 62	Report from the Pharmaceutical Journal

14.	Pharmacist-based medication review reduces potential drug-related problems in the elderly: the SMOG controlled trial. Vinks, T, Egberts, T, De Lange, T, De Koning F. <i>Drugs and Aging</i> . 2009.26 (2) 123-133	Full article obtained. No screening tool used. Medication review used. Drug Related Problems were identified and validated by reference to national prescribing guidelines such as the Practice Standards of Dutch GPs as well as therapeutic handbooks
15.	Efficacy of a clinical medication review on the number of potentially inappropriate prescriptions prescribed for community-dwelling elderly people. Allard, J, Hebert, R, Rioux, Voyer, L. <i>Canadian Medical Association journal</i> . 2001. 164. 9. 1291-6.	Full article obtained. Potentially Inappropriate Prescriptions (PIPs) were identified from a list of PIPs developed by the Quebec Committee on Drug Use in the Elderly. Although generated by a panel of experts, this list has never been validated with empirical data.
16.	The MEDMAN study: A randomized controlled trial of community pharmacy-led medicines management for patients with coronary heart disease. The Community Pharmacy Medicines Management Project Evaluation Team. <i>Family Practice</i> . 2007. 24, 189-200.	Full article obtained No screening tool used.
17.	Drug Burden Index and potentially inappropriate medications in community-dwelling older people: the impact of Home Medicines Review. Castelino RL, Hilmer SN, Bajorek BV, Nishtala P, Chen TF. <i>Drugs and Aging</i> . 2010; 27(2):135-48.	From abstract: A retrospective analysis of medication reviews. No control group. Full article not required.
18.	The cost-effectiveness of a clinical pharmacist intervention among elderly outpatients. Cowper PA, Weinberger M, Hanlon JT, Landsman PB, Samsa GP, Uttech KM, <i>et al</i> . <i>Pharmacotherapy</i> . 1998 Mar-Apr;18(2):327-32	Full article obtained Cost analysis of a previously reported randomised controlled trial (A randomised controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. Hanlon <i>et al</i> . 1996. This paper was included in our final review)
19.	Retrospective evaluation of medication appropriateness and clinical pharmacist drug therapy recommendations for home-based primary care veterans. Davis RG, Hepfinger CA, Sauer KA, Wilhardt MS. <i>American Journal of Geriatric Pharmacotherapy</i> . 2007 3//; 5(1):40-7	Full article obtained: Hard copy only Retrospective analysis. No control group.

20.	Treatment reviews of older people on polypharmacy in primary care: cluster controlled trial comparing two approaches. Denneboom W, Dautzenberg MG, Grol R, De Smet PA. <i>British Journal of General Practice</i> . 2007; 57(542):723-31	Full article obtained Treatment review only. No screening tool used.
21.	Pharmaceutical care for elderly patients in community pharmacy: analysis and evaluation of community pharmacist interventions in the Randomised Evaluation of Shared Prescribing for Elderly People in the Community over Time (RESPECT) Study. Faya S. Ann Arbor: University of Bradford (United Kingdom); 2009.	Paper produced as part of PhD thesis. Thesis obtained
22.	Effect of nurse practitioner and pharmacist counselling on inappropriate medication use in family practice. Fletcher J, Hogg W, Farrell B, Woodend K, Dahrouge S, Lemelin J, et al. <i>Canadian Family Physician</i> . 2012; 58(8):862-8.	Full article obtained This study had no control group
23.	Appropriate medications: prescription and use in primary care. Goodyear-Smith F. <i>Journal of primary health care</i> . 2013 Sep; 5(3):178-9.	Full article obtained Not relevant: Editorial review
24.	Impact of a pharmaceutical care model for non-institutionalised elderly: Results of a randomised, controlled trial. Grymonpre RE, Williamson DA, Montgomery PR. <i>International Journal of Pharmacy Practice</i> . 2001;9:235-41.	Full article obtained Not related to inappropriate prescribing
25.	Description and process evaluation of pharmacists' interventions in a pharmacist-led information technology-enabled multicentre cluster randomised controlled trial for reducing medication errors in general practice (PINCER trial). Howard R, Rodgers S, Avery AJ, Sheikh A. <i>International Journal of Pharmacy Practice</i> . 2014; 22(1):59-68.	Full article obtained Pharmacist's recommendations to manage individual cases of hazardous medicines management. No screening tool used.
26.	Effect of prescriber education on the use of medications contraindicated in older adults in a managed Medicare population. Kaufman MB, Brodin KA, Sarafian A. <i>Journal of Managed Care Pharmacy</i> . 2005 Apr; 11(3):211-9.	Full article obtained This was a before and after study. No control group

27.	Pharmacist-led medication review in patients over 65: A randomized, controlled trial in primary care. Krska J, Cromarty JA, Arris F, Jamieson D, Hansford D, Duffus PRS, <i>et al. Age and Ageing</i> . 2001; 30(3):205-11.	Full article obtained The study identified pharmaceutical care issues using medication reviews, however no screening tool used.
28.	The effect of home medication review on the resolution of drug related problems and health-related quality of life. Kwint HF, Faber A, Bouvy ML. <i>International Journal of Clinical Pharmacy</i> . 2013;35(5):896	Article obtained Poster presented at 41st European Society of Clinical Pharmacy symposium on clinical pharmacy: Barcelona, Spain. 29–31 October 2012
29.	Effects of medication review on drug-related problems in patients using automated drug-dispensing systems: A pragmatic randomized controlled study. Kwint HF, Faber A, Gussekloo J, Bouvy ML. <i>Drugs and Aging</i> . 2011; 28(4):305-14.	Full article obtained Medication review. Implicit and explicit criteria used. Explicit criteria consisted of a list of clinical rules based on Dutch treatment and prescription guidelines. Implicit criteria for identifying Drug Related Problems were based on a structural assessment by Cipolle according to a rational order of indication, effectiveness, safety and compliance.
30.	Assessing the appropriateness of physician prescribing for geriatric outpatients: Development and testing of an instrument. Lipton HL, Bird JA, Bero LA, McPhee SJ. <i>Journal of Pharmacy Technology</i> . 1993; 9(3):107-13.	Full article obtained: Hard copy only. This study was carried out in secondary care. It involved the development and testing of an instrument for drug therapy prescribing problems for geriatric patients.
31.	Inappropriate prescribing predicts adverse drug events in older adults. Lund BC, Carnahan RM, Egge JA, Chrischilles EA, Kaboli PJ. <i>The Annals of pharmacotherapy</i> . 2010 Jun; 44(6):957-63.	Full article obtained Study utilised data from a previous study (The Veterans Affairs Enhanced Pharmacy Outpatient Clinic (EPOC) study: a randomised controlled pharmacist- physician intervention trial. Kaboli <i>et al.</i> 2004). Objective: To determine whether an implicit measure of inappropriate prescribing can predict ADE risk. MAI score not segregated between control and intervention group.
32.	An educational intervention to reduce the use of potentially inappropriate medications among older adults (EMPOWER study): protocol for a cluster randomized trial. Martin P, Tamblyn R, Ahmed S, Tannenbaum C. <i>Trials</i> . 2013, 14:80. 1-11.	Full article obtained. Educational intervention. Outcome: Cessation of benzodiazepines in the 6 months following receipt of the intervention. Trial ongoing currently recruiting patients.

33.	Improving the quality of pharmacotherapy in elderly primary care patients through medication reviews: a randomised controlled study. Milos V, Rekman E, Bondesson A, Eriksson T, Jakobsson U, Westerlund T, et al. <i>Drugs & Aging</i> . 2013 Apr;30(4):235-46	Full article obtained. The majority of the patients in the present study were living in nursing homes. The goal of medication reviews has been improved patient safety and quality of medication use, according to the Swedish National Board of Health and Welfare's indicators for good drug therapy in the elderly.
34.	Physicians and pharmacists: collaboration to improve the quality of prescriptions in primary care in Mexico. Mino-Leon D, Reyes-Morales H, Jasso L, Douvoba SV. <i>International Journal of Clinical Pharmacy</i> . 2012 Jun; 34(3):475-80.	Full article obtained. Aim to reduce prescription errors for patients with diabetes and/or hypertension. No screening tool used.
35.	Inappropriate Drug Prescribing and Polypharmacy Are Major Causes of Poor Outcomes in Long-Term Care. Morley JE. <i>Journal of the American Medical Directors Association</i> . 2014 11//; 15(11):780-2.	Not relevant: Study carried out in Long term care i.e. nursing homes
36.	Evaluation of studies investigating the effectiveness of pharmacists' clinical services (Structured abstract). Morrison A, Wertheimer AI. <i>American Journal of Health-System Pharmacy</i> . 58. 7. 569-577	Not relevant: systematic review
37.	Implantation of a program for polymedicated patients within the framework of the Galician Strategy for Integrated Chronic Care. Reboredo-Garcia S, Mateo CG, Casal-Llorente C. <i>Atencion Primaria</i> . 2014; 46 Suppl 3:33-40.	Full article obtained Published in Spanish. (A native Spanish speaker was recruited to translate the article into English, Dec 2014.) No control study
38.	Polypharmacy and health beliefs in older outpatients. Rossi MI, Young A, Maher R, Rodriguez KL, Appelt CJ, Perera S, et al. <i>American Journal Geriatric Pharmacotherapy</i> . 2007; 5(4):317-23.	Abstract only. This study contained no control group.
39.	Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. Schmader KE, Hanlon JT, Pieper CF, Sloane R, Ruby CM, Twersky J, et al. <i>The American Journal of Medicine</i> . 2004 3/15//; 116(6):394-401.	Full article obtained Analysed same patients as inpatient and outpatients.

40.	A randomized controlled trial of a pharmacist consultation program for family physicians and their elderly patients (Structured abstract). Sellors J, Kaczorowski J, Sellors C, Dolovich L, Woodward C, Willan A, <i>et al.</i> <i>Canadian Medical Association Journal</i> . 2003; 169(1):17-22	Full article obtained. The intervention focused on drug related problems. The primary end-point measure was a reduction in the daily units of medication taken, as a surrogate for optimized drug therapy.
41.	Potentially Inappropriate Medications in Community-Dwelling Older Adults. Shade MY, Berger AM, Chaperon C. <i>Research in Gerontological Nursing</i> . 7. 4. 178-192	Full article obtained This is a systematic review.
42.	Implementation of medication reviews in community pharmacies and their effect on potentially inappropriate drug use in elderly patients. Teichert M, Luijben SN, Wereldsma A, Schalk T, Janssen J, Wensing M, <i>et al.</i> <i>International Journal of Clinical Pharmacy</i> . 2013; 35(5):719-26.	Full article obtained. Specifically developed algorithms were used to identify nine potentially inappropriate medicines (PIMs) from the HARM study
43.	Pharmaceutical care for elderly patients shared between community pharmacists and general practitioners: a randomised evaluation. RESPECT (Randomised Evaluation of Shared Prescribing for Elderly people in the Community over Time. Wong I, Campion P, Coulton S, Cross B, Edmondson H, Farrin A, <i>et al.</i> <i>BMC Health Services Research</i> .. 2004. 4(1). 11	Full article obtained This paper describes a proposed randomised multiple interrupted time series trial design.
44.	Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: a randomised controlled trial. Zermansky AG, Petty DR, Raynor DK, Lowe CJ, Freemantle N, Vail A. <i>Health Technology Assessment</i> (Winchester, England). 2002; 6(20):1-86.	Full article obtained Primary outcome: the number of repeat medication changes per patient over a 12 month period. Secondary outcome was the effect on the medication costs.
45.	Impact of an enhanced pharmacy discharge service on prescribing appropriateness criteria: a randomised controlled trial. Basger B.J, Moles R.J, Chen T.F. <i>International Journal of Clinical Pharmacy</i> . (2015). 37: 1194-1205.	Full article obtained. This study was performed in a small private hospital. (Not a primary care study).
46.	The WestGem study; Medication management in the elderly. Rose O, Waltering I, John C, Mertens-Keller D, Richling I, Koeberlein-Neu J. <i>International Journal of Clinical Pharmacy</i> . 2015; 37(2):405-6.	Abstract only obtained. The WestGem-Study is still going on, results will be published by the end of 2015.
47.	Majority of drug-related problems identified during medication review are not associated with STOPP/START criteria. Verdoorn S, Kwint HF, Faber A, Gussekloo J, Bouvy ML. <i>European Journal of Clinical Pharmacology</i> . 2015 Oct; 71(10):1255-62.	Full article obtained. This study has no control group.

48.	<p>Combined intervention programme reduces inappropriate prescribing in elderly patients exposed to polypharmacy in primary care. Bregnhøj L, Thirstrup S, Kristensen MB, Bjerrum L, Sonne J. <i>European Journal of Clinical Pharmacology</i>. (2009) 65:199–207.</p>	<p>Full article obtained</p> <p>This was not a pharmacist-led study. The pharmacist analysed the patients' prescription and medical history and proposed changes in their medication. The pharmacist and clinical pharmacologist discussed these recommendations, however it was the responsibility of the clinical pharmacologist what was finally recommended. The pharmacist forwarded the feedback to the physicians. The clinical pharmacologists contacted the physicians by telephone to discuss any uncertainties concerning the recommendations given. The clinical pharmacologists delivered the interactive educational interventions.</p>
49.	<p>Improving prescribing patterns for the elderly through an online drug utilization review intervention. A System Linking the Physician, Pharmacist, and Computer. Monane, M, Matthias, D, Nagle, B, Kelly, M. <i>Journal of the American Medical Association</i>. 1998;280(14):1249-1252</p> <p><u>*Hand searched</u></p>	<p>Full article obtained.</p> <p>This study has no control group.</p>
50.	<p>A randomized study to decrease the use of potentially inappropriate medicines among community-dwelling older adults in a south-eastern managed care organisation. Fick DM, Maclean JR, Rodriguez NA, Short L, Heuvel RV, Waller JL, Rogers RL. <i>American Journal of Managed Care</i>. 2004 Nov; 10(11 Pt 1):761-8.</p> <p><u>*Hand searched</u></p>	<p>Full article obtained.</p> <p>Pharmacists suggested a list of potentially inappropriate medicine alternative medicines and performed a peer review of the drugs to be included in the intervention and their corresponding alternative medications.</p> <p>Not a pharmacist led intervention.</p>
51.	<p>Pharmacist's contribution in a heart function clinic: patient perception and medication appropriateness. Bucci, C, Jackevicius, C, McFarlane, K, Liu, P. <i>Canadian Journal of Cardiology</i> 2003; 19(4):391–6.</p> <p><u>*Hand searched</u></p>	<p>Full article obtained.</p> <p>This pharmacist intervention was carried out at the heart function clinic at Toronto General Hospital. Interventions carried out in secondary care were not included in the review</p>
52.	<p>Meredith S, Feldman P, Frey D, Giammarco L, Hall K, Arnold K, et al. Improving medication use in newly admitted home healthcare patients: A randomized controlled trial. <i>Journal of the American Geriatric Society</i>. 2002; 50:1484-1491.</p> <p><u>*Hand searched</u></p>	<p>Full article obtained</p> <p>There was no validated screening tool used in this study and potentially inappropriate prescribing was not measured as an outcome.</p>

53.	<p>Avorn J, Soumerai SB. Improving drug-therapy decisions through educational outreach. A randomized controlled trial of academically based "detailing". <i>New England Journal of Medicine</i>. 1983 Jun 16; 308(24):1457-63.</p> <p><u>*Hand searched</u></p>	<p>Full article obtained</p> <p>The three target drugs were selected on the basis of an analysis of national prescribing practices i.e. Medicaid prescribing records and evidence from published controlled clinical trials. There was no screening tool used in the intervention and the target population was not specifically aimed at those aged 65 and older.</p>
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Supplementary material 5. PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	69
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.	70-71
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	72-74
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	74
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (i.e., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (i.e., PICOS, length of follow-up) and report characteristics (i.e., years considered, language, publication status) used as criteria for eligibility, giving rationale.	75-76
Information sources	7	Describe all information sources (i.e., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	74-75
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	74-75
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).	75-77
Data collection process	10	Describe method of data extraction from reports (i.e., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	75-77

Data items	11	List and define all variables for which data were sought (i.e., PICOS, funding sources) and any assumptions and simplifications made.	75-77
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.	77
Summary measures	13	State the principal summary measures (i.e. risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (i.e., I^2) for each meta-analysis.	N/A

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (i.e., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (i.e., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	77-78
Study characteristics	18	For each study, present characteristics for which data were extracted (i.e., study size, PICOS, follow-up period) and provide the citations.	79-88
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	89-91
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	89-91
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (i.e., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (i.e., healthcare providers, users, and policy makers).	92-93
Limitations	25	Discuss limitations at study and outcome level (i.e., risk of bias), and at review-level (i.e., incomplete retrieval of identified research, reporting bias).	99
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	100
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (i.e., supply of data); role of funders for the systematic review.	N/A

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Appendix III. Supplementary material for Chapter 5.

Supplementary material 6. Example of topic guides

The topic guide was iteratively refined as the study progressed to pursue emerging themes. Examples of topic guides 1 and 7 are presented below.

Topic guide 1

1. How do you think prescribing for patient's aged 65 and older differs from prescribing for the general adult population?
2. What resources would you use for prescribing in this group of patients?
3. What are the challenges you face to prescribing for those over 65?
4. What are the adverse consequences to prescribing to those over 65?
5. Do you think that prescribing in general practice can impact on your relationship with other healthcare professionals? Can you think of an example?
6. Would you use other healthcare professionals as resources when prescribing for this group of patients? Would you seek the opinion of other healthcare professionals?
When is this useful?
When is it not useful?
7. What kind of strategies do you think could assist your prescribing in general practice?
What do you think of Clinical Decision Support Systems (CDSS)?
8. How could the pharmacist have a role in optimising prescribing in primary care?
9. How could pharmacist's and GPs work together when it comes to prescribing in ≥ 65 years?
10. Any further comments?

Topic guide 7

1. How do you think prescribing for patient's aged 65 and older differs from prescribing for the general adult population?
2. As you know, the population of older people is increasing. How do you think this is going to affect your role as a GP in the future?
3. From your experience does your surrounding environment impact on your prescribing for older patients? Can you give an example? Prompts i.e. Time constraints, patient education etc.
4. When you are prescribing for older patients, what are you thinking about and considering? Some GPs have mentioned that prescribing benzodiazepines or sleeping tablets can be an issue?
5. What sources of information would you use for prescribing in older patients? Where would you look for prescribing information? I.e. guidelines
6. Would you use other healthcare professionals as resources when prescribing for this group of patients? Would you seek the opinion of other healthcare professionals?
When is this useful?
When is it not useful?
7. Do you think that prescribing in general practice can impact on your relationship with other healthcare professionals? If so, how?
8. Do you think that other healthcare professionals form a judgement on your prescribing for older patients? Is this a concern for you?
9. How would you feel if a prescribing mistake was highlighted to you by another healthcare professional? Would you feel comfortable changing it?
10. What would you think of an educational presentation delivered by community pharmacists to GPs to highlight their prescribing patterns in primary care? Would you find it beneficial? I.e. Academic detailing?

11. How could the community pharmacist have a role in optimising prescribing in primary care? I.e. carrying out medication reviews.
12. How would you feel if the role of the community pharmacist was expanded in primary care?
13. How could pharmacist's and GPs work together when it comes to prescribing in those ≥ 65 years?
14. Any further comments?

Supplementary material 7. Table of consolidated criteria for reporting qualitative studies (COREQ) checklist.

Item No	Guide questions/description	Response
Domain 1 : Research team and reflexivity		
Personal characteristics		
1. Interviewer	Which author/s conducted the interview?	The primary author D.O.R. conducted the interviews.
2. Credentials	What were the researcher's credentials? I.e. PhD	D.O.R. is a research pharmacist/PhD student.
3. Occupation	What was their occupation at the time of the study?	Full time research pharmacist in Clinical Pharmacy in an academic institution.
4. Gender	Was the researcher male or female?	Male
5. Experience & training	What experience or training did the researcher have?	D.O.R. received training at the Health Experience Research Group, Oxford University and completed training in NVivo computer assisted qualitative data management.
Relationship with participants		
6. Relationship established prior to study commencement	Was a relationship established prior to study commencement?	No
7. Participant knowledge of the interviewer	What did the participants know about the researcher?	Yes in a minority of cases (2 GPs).
8. Interviewer characteristics	What characteristics were reported about the interviewer? i.e. Bias, assumptions, reasons and interests in the research topic	Not addressed.
Domain 2: Study design		
Theoretical framework		
9. Methodological orientation & theory	What methodological orientation was stated to underpin the study?	Open coding mapped to the TDF*.
Participant selection		
10. Sampling	How were participants selected? i.e. purposive, convenience, consecutive, snowball	Purposive sampling was complemented by snowball sampling where necessary.
11. Method of approach	How were participants approached? i.e. face-to-face, telephone, mail, email	D.O.R. contacted potential participants by telephone and a brief summary of the study was given.

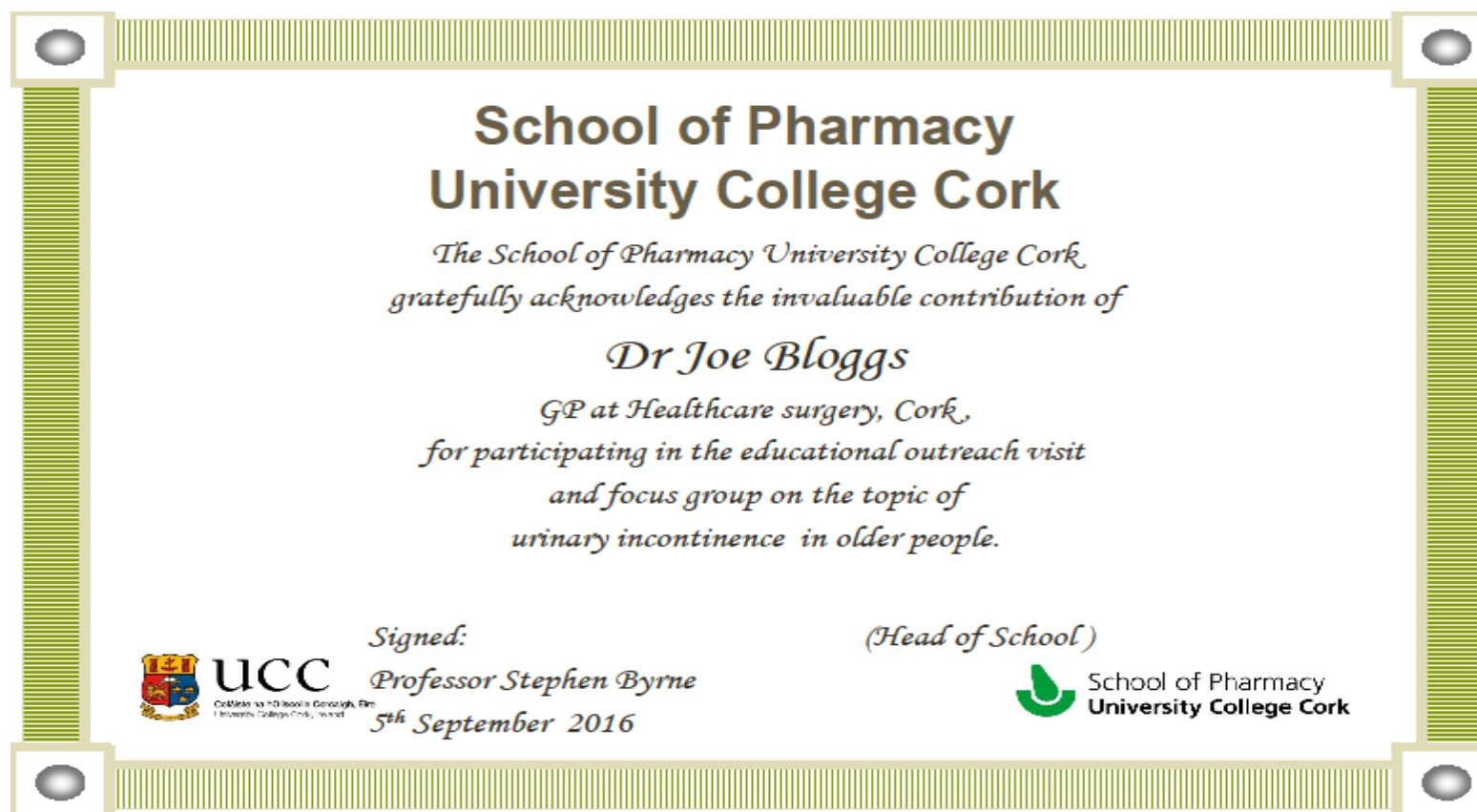
12. Sample size	How many participants were in the study?	16
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Not applicable: participation was voluntary.
14. Setting of data collection	Where was the data collected? i.e. home, clinic, workplace	In the GP participants surgeries.
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	No
16. Description of sample	What are the important characteristics of the sample? I.e. demographic data, date.	See Table 5.1.
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	The first two interviews were reviewed for interview technique. The topic guide was reviewed after each interview.
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	No
19. Audio/visual recording	Did the researcher use audio or visual recording to collect the data?	Data were audio recorded using a digital voice recorder.
20. Field notes	Were field notes made during and/or after the interview?	Yes. Field notes were taken immediately after each interview.
21. Duration	What was the duration of the interviews?	The mean interview length was 19 min (Range 9-31 min).
22. Data saturation	Was data saturation discussed?	Data saturation was reached at interview number 16.
23. Transcripts returned	Were transcripts returned to participants for comment?	No, but they were available to participants on request.
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	Three coders coded the data.
25. Description of coding tree	Did authors provide a description of the coding tree?	No coding tree was developed but all the researchers discussed and agreed on the framework analysis approach <i>a priori</i> .
26. Derivation of themes	Were themes identified in advance or derived from the data?	Themes were derived from the data by open coding and then mapped to the TDF.

27. Software	What software, if applicable, was used to manage the data?	NVivo Qualitative Data Analysis Software V.10.22 was used.
28. Participant checking	Did participants provide feedback on the findings?	No
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings?	Yes. Supporting quotations from GPs are presented.
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Quotes are embedded in text and are used to illustrate our findings in participants own language as much as possible.
31. Clarity of major themes	Were major themes clearly presented in the findings?	Major themes are presented in the results section.
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Variations in views and themes and minor themes are presented.

*TDF= Theoretical Domains Framework

Appendix IV. Supplementary material for Chapter 6

Supplementary material 8. GP certificate of participation



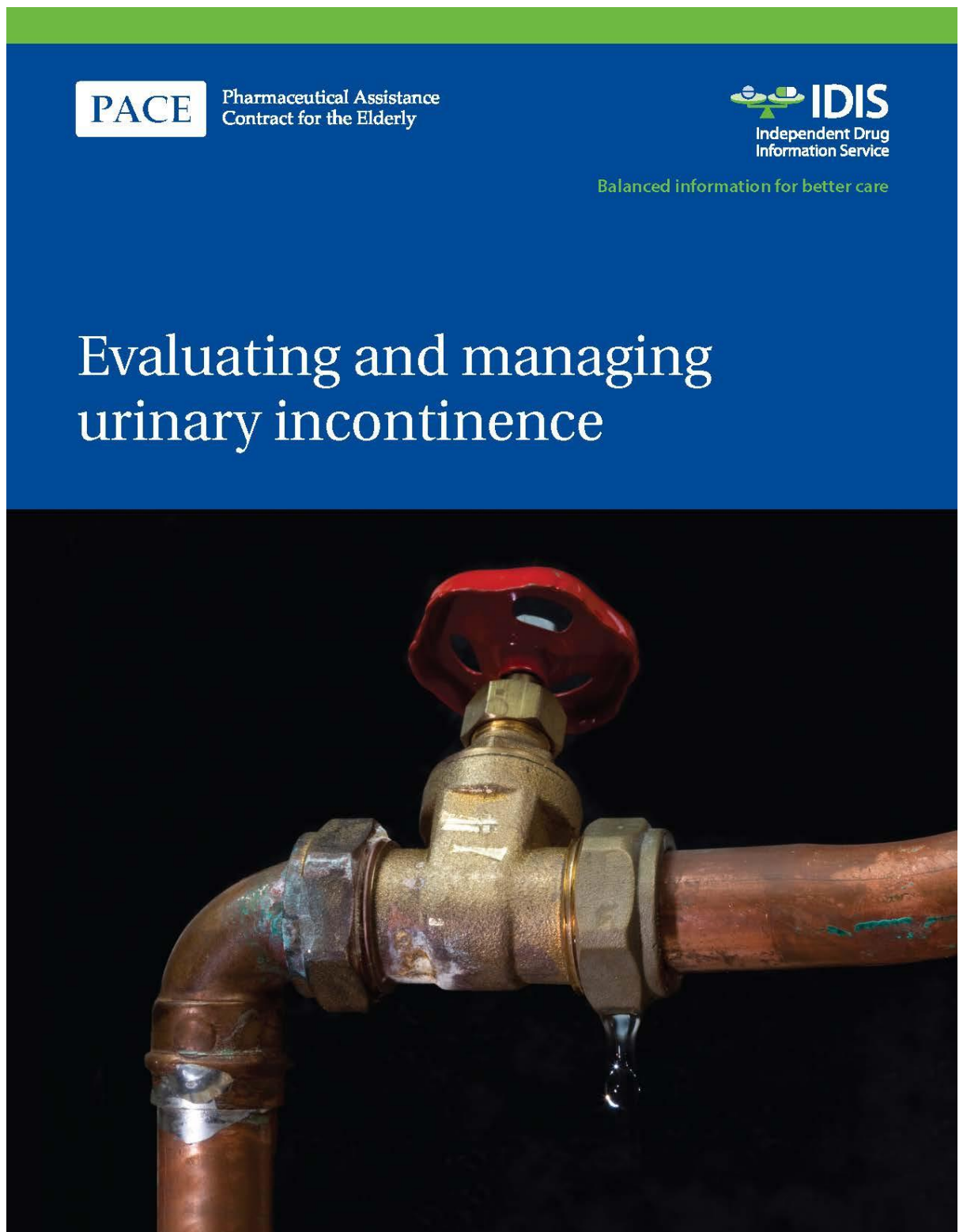
Supplementary material 9. CPD certificate



CONTINUING PROFESSIONAL DEVELOPMENT: RESEARCH POINTS			
Name of GP: Dr X			
Name of Researcher: Mr David O Riordan, research pharmacist, University College Cork.			
Date of research meeting	Purpose of research meeting	Duration of meeting	GP Signature
8 th July 2016	Participation in an educational outreach visit on urinary incontinence in older people.	15 minutes	
21 st July 2016	Participation in a qualitative focus group to assess the feasibility and satisfaction of the educational outreach visit.	25 minutes	

CONTINUING PROFESSIONAL DEVELOPMENT: INTERNAL POINTS			
Internal CPD Activity: Clinical chart review of diagnoses and treatments for urinary incontinence in older people.			
Date of chart review	Patient initials/ date of birth	Duration of review	GP Signature

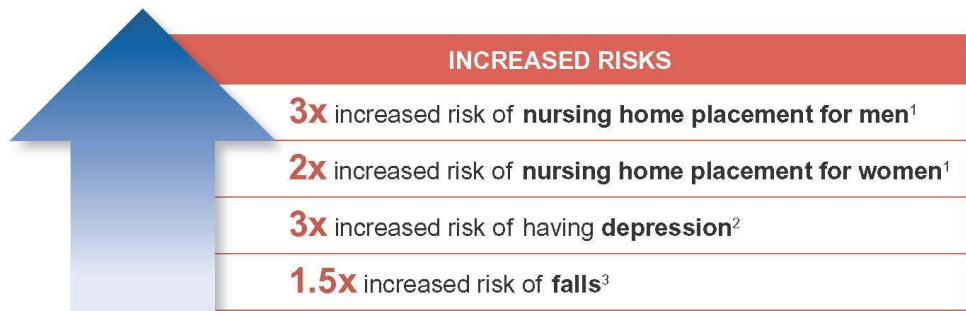
1 hour of activity = 1 CPD point



Urinary incontinence: major impact, but few seek care

It is *not* a normal part of aging.

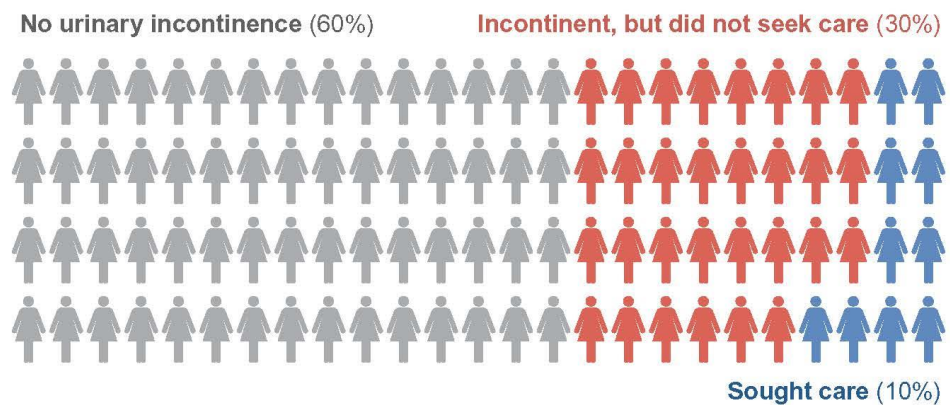
FIGURE 1. Incontinence raises the risk of important clinical events.



Incontinence is also expensive, with an annual direct cost of \$19 billion.⁴

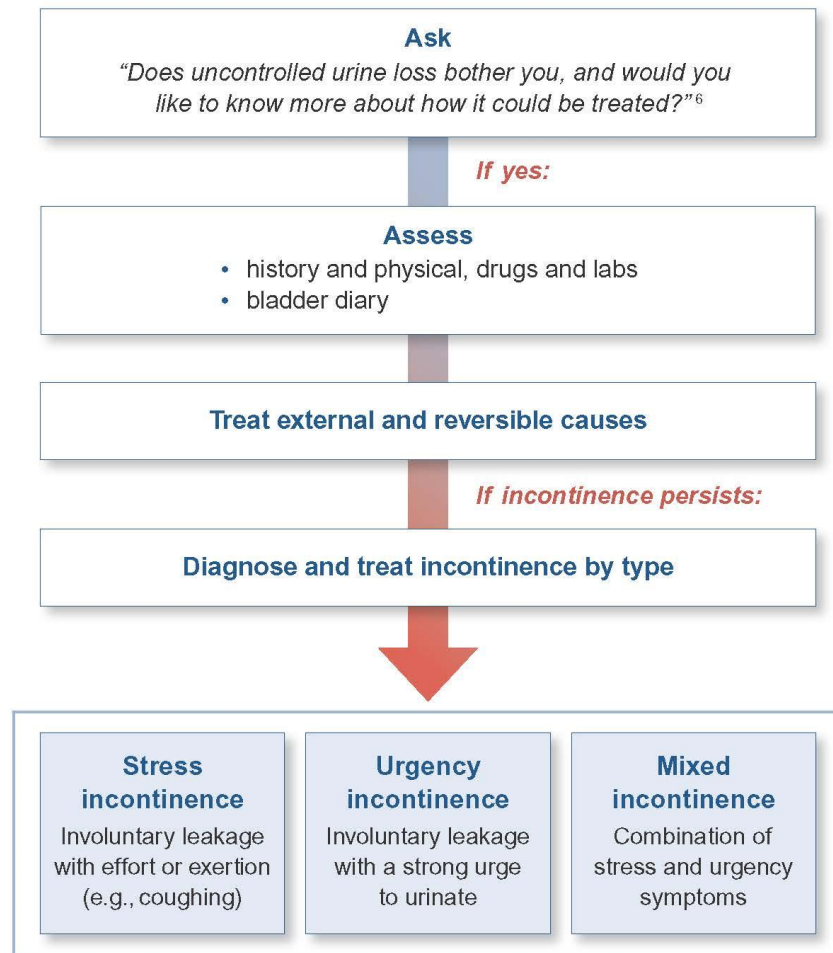
Patients may be unwilling to talk about incontinence, often suffering needlessly.

FIGURE 2. Despite the high prevalence of incontinence, most patients do not seek or receive care.⁵



A straightforward workup can guide effective treatment

FIGURE 3. Algorithm for detecting and addressing incontinence



If incontinence persists or an anatomical abnormality is suspected, refer to a urologist or urogynecologist.

Finding reversible causes of incontinence can make a big difference

FIGURE 4. Factors contributing to incontinence

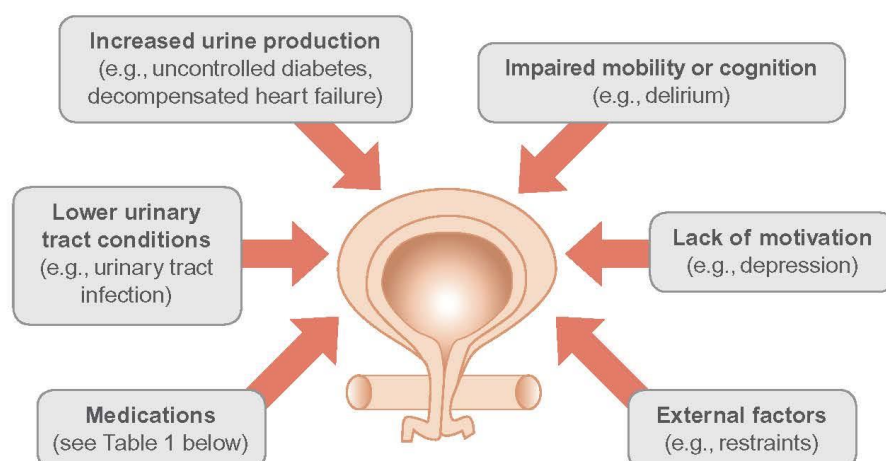





















































TABLE 1. Medications that can affect continence




Effect on continence	Drug class
urinary retention	α -agonists, anticholinergics, antidepressants, antipsychotics, calcium channel blockers, inhaled anticholinergics, opioids
sedation, delirium, immobility	alcohol, anticholinergics, antidepressants, antipsychotics, opioids, sedative-hypnotics
increased urine production	alcohol, caffeine, diuretics
urethral muscle relaxation	α -blockers, sedative-hypnotics
stool impaction	anticholinergics, opioids
cough	ACE inhibitors
bladder irritation	caffeine

Evidence overview of interventions to treat incontinence

TABLE 2. Behavioral and pharmacologic treatments of incontinence in men and women

Interventions	Stress UI	Urgency UI	Mixed UI
BEHAVIOR (first-line treatment)			
caffeine reduction	 	 	 
pelvic floor muscle training	 	 	 
bladder training	 	 	 
weight loss (<i>for obese patients</i>)	 	 	 
MEDICATIONS (second-line treatment)			
anticholinergics	 	 	 
β_3-adrenoceptor agonists	 	 	 
duloxetine	 	 	 
α_1-adrenoceptor antagonists	 	 	 
vaginal estrogen			

 = men  = women

-  = efficacy and acceptable safety
-  = efficacy but unfavorable/unclear safety
-  = not efficacious or insufficient evidence

Stress incontinence in women can respond to behavioral interventions

Caffeine and fluid reduction are often recommended, but their effectiveness in reducing stress incontinence is limited.⁷

TABLE 3. Effective strategies to manage stress incontinence

Interventions	Relative reduction in incontinence	Number need to treat for benefit*	Absolute reduction in incontinence
BEHAVIOR			
pelvic floor muscle training (Kegel exercises) ⁸⁻¹²	54-74%	1 in 2	50%
weight loss ¹³	58%	1 in 5	20%
MEDICATIONS			
vaginal estrogen ¹⁴		1 in 5	20%

* Proportion of treated women who have a $\geq 50\%$ reduction in incontinence episodes

Medications have only a limited role in managing stress incontinence.

- Trials have not produced evidence that systemic drugs improve stress incontinence.¹² Oral estrogen actually worsens incontinence.¹⁵
- Vaginal estrogen has limited data for efficacy in stress incontinence and carries an FDA warning related to risks such as breast cancer and thromboembolic disease.

Urgency incontinence in women: start with behavioral interventions, use medications with caution

TABLE 4. Effective strategies to manage urgency incontinence

Interventions	Relative reduction in incontinence	Number need to treat for benefit*	Absolute reduction in incontinence
BEHAVIOR			
caffeine reduction ¹⁶	55%		
bladder training ^{12,17,18}	46-57%	1 in 2	50%
weight loss ¹³	42%	1 in 6	17%
MEDICATIONS			
anticholinergics ^{12,19}	60%	1 in 6-10	10-17%
β_3 -adrenoceptor agonist ^{12,20}	55%	1 in 9	11%
vaginal estrogen ¹⁴		1 in 2	50%

* Proportion of treated women who have a $\geq 50\%$ reduction in incontinence episodes

Anticholinergic drugs: similar efficacy, but their adverse effect rates vary widely.

- Common side effects: dry mouth (10-70%), constipation (2-20%), headache (2-8%).
- Extended-release preparations are better tolerated.

β_3 -Adrenoceptor agonist (mirabegron [Myrbetriq])

- Has efficacy similar to that of anticholinergics, but data on long-term safety are limited.
- Common side effects: elevated blood pressure (9-11%), heart rate (2%), nasopharyngitis (4%), urinary tract infection (3-6%).

Not all “overactive bladder” results in incontinence or requires medication.

Overactive bladder, characterized by urgency and frequency, does not always cause loss of urine, and does not always require drug treatment.

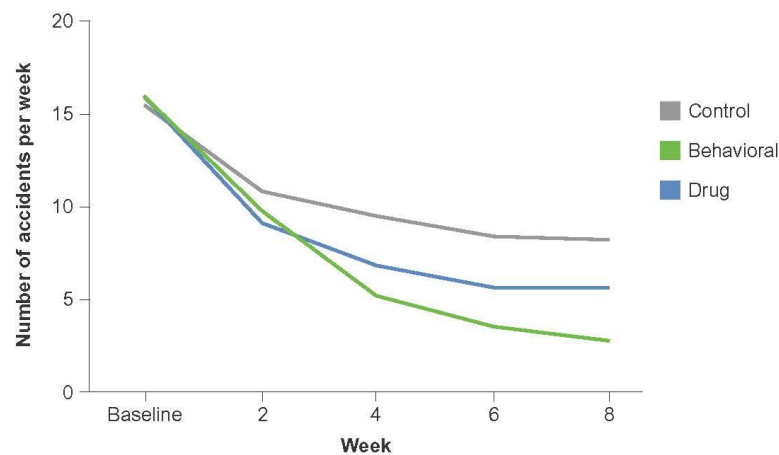
For mixed incontinence in women, match treatment to the primary symptom

Mixed incontinence is not a distinct entity; it has components of stress and urgency incontinence.

Patients report better satisfaction with behavioral treatment (78%) than drugs alone (49%).²¹



FIGURE 5. Behavioral training may be more effective than drugs in older women.²¹



Anticholinergic medications can help in urgency-dominant but not stress-dominant mixed incontinence.

There is less evidence on treating incontinence in men

Urgency incontinence is the most common type of male incontinence.

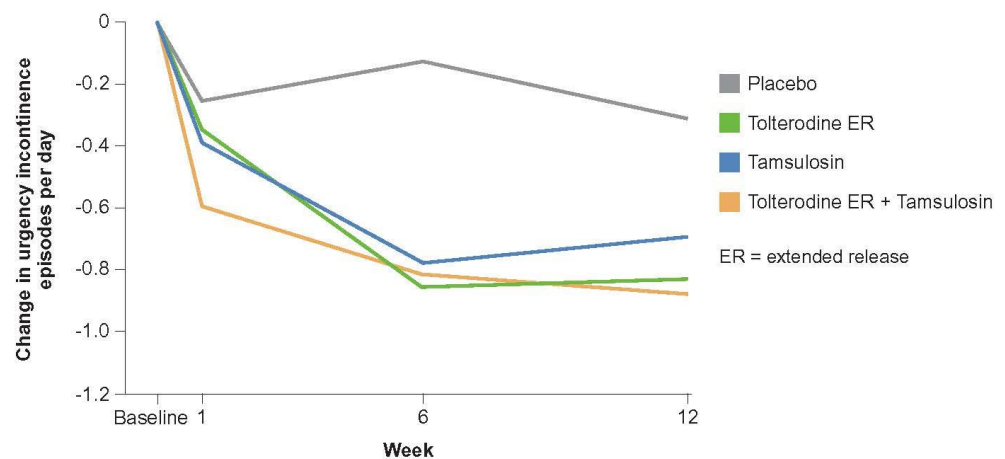
Behavioral interventions work:

- Weight loss: a 9% reduction in weight led to a 56% reduction in incontinence.²²

Pharmacologic interventions:

- Behavioral interventions such as bladder training are as effective as anticholinergics in men taking α -blockers.²³

FIGURE 6. α -blockers, anticholinergics, and their combination are similarly effective in reducing incontinence episodes.²⁴

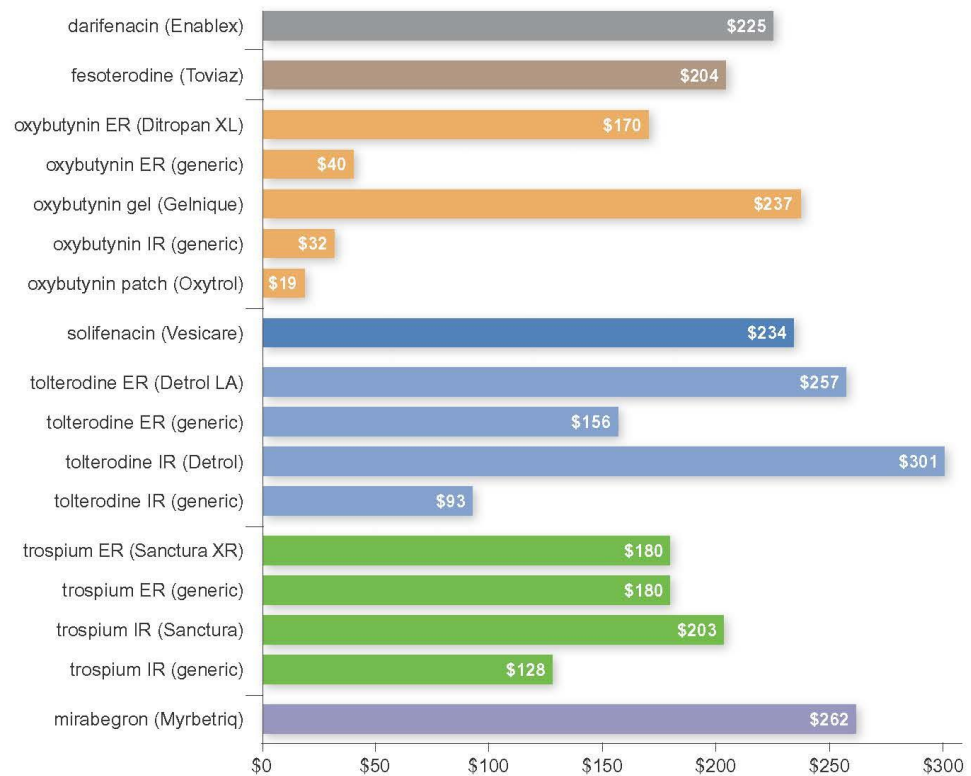


Stress incontinence in men:

- No behavioral or pharmacological interventions have been proven effective.
- Persistent post-prostatectomy stress incontinence may benefit from specialist referral.

Drug costs vary widely, and can be quite high

FIGURE 7. Price for a month's supply of medications for incontinence



ER = extended release, IR = immediate release

Prices are generally similar across different doses. Source: goodrx.com

Links to resources for talking with patients about incontinence and more at:
alosafoundation.org/modules/incontinence

Key messages

- Urinary incontinence is common and can have a substantial clinical impact, including reduced quality of life, depression, and nursing home admission.
- It is **not** a normal part of aging.
- Simple screening can reveal symptoms that might otherwise go undetected and untreated.
- Look for and manage reversible causes of incontinence.
- Distinguish among urgency, stress, mixed, and other causes to guide treatment.
- As appropriate, implement caffeine reduction, pelvic floor muscle training, bladder training, and weight loss as first-line treatments.
- Medications can be useful to treat urgency symptoms, but not those of stress incontinence. They often have modest benefits, variable side effects, and (occasionally) enormous costs.

References:

- (1) Thom DH, Haan MN, Van Den Eeden SK. Medically recognized urinary incontinence and risks of hospitalization, nursing home admission and mortality. *Age Ageing*. 1997;26(5):367-374. (2) Melville JL, Delaney K, Newton K, Katon W. Incontinence severity and major depression in incontinent women. *Obstet Gynecol*. 2005;106(3):585-592. (3) Chiarelli PE, Mackenzie LA, Osmotherly PG. Urinary incontinence is associated with an increase in falls: a systematic review. *Aust J Physiother*. 2009;55(2):89-95. (4) Hu TW, Wagner TH, Bentkover JD, Leblanc K, Zhou SZ, Hunt T. Costs of urinary incontinence and overactive bladder in the United States: a comparative study. *Urology*. 2004;63(3):461-465. (5) Minassian VA, Yan X, Lichtenfeld MJ, Sun H, Stewart WF. The iceberg of health care utilization in women with urinary incontinence. *Int Urogynecol J*. 2012;23(8):1087-1093. (6) Wenger NS, Roth CP, Shekelle PG, et al. A practice-based intervention to improve primary care for falls, urinary incontinence, and dementia. *J Am Geriatr Soc*. 2009;57(3):547-555. (7) Swithinbank L, Hashim H, Abrams P. The effect of fluid intake on urinary symptoms in women. *J Urol*. 2005;174(1):187-189. (8) Lagro-Janssen TL, Debruyne FM, Smits AJ, van Weel C. Controlled trial of pelvic floor exercises in the treatment of urinary stress incontinence in general practice. *Gr J Gen Pract*. 1991;41(352):445-449. (9) Burns PA, Pranikoff K, Nochajski TH, Hadley EC, Levy KJ, Ory MG. A comparison of effectiveness of biofeedback and pelvic muscle exercise treatment of stress incontinence in older community-dwelling women. *Journal Gerontol*. 1993;48(4):M167-174. (10) Bo K, Talseth T, Holme I. Single blind, randomised controlled trial of pelvic floor exercises, electrical stimulation, vaginal cones, and no treatment in management of genuine stress incontinence in women. *BMJ*. 1999;318(7182):487-493. (11) Castro RA, Arruda RM, Zanetti MR, Santos PD, Sartori MG, Girao MJ. Single-blind, randomized, controlled trial of pelvic floor muscle training, electrical stimulation, vaginal cones, and no active treatment in the management of stress urinary incontinence. *Clinics (Sao Paulo, Brazil)*. 2008;63(4):465-472. (12) Qaseem A, Dallas P, Forciea MA, et al. Nonsurgical management of urinary incontinence in women: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2014;161(6):429-440. (13) Subak LL, Wing R, West DS, et al. Weight loss to treat urinary incontinence in overweight and obese women. *N Engl J Med*. 2009;360(5):481-490. (14) Cody JD, Jacobs ML, Richardson K, Moehrer B, Hextall A. Oestrogen therapy for urinary incontinence in post-menopausal women. *Cochrane Database Syst Rev*. 2012;10:Cd001405. (15) Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. *JAMA*. 2005;293(8):935-948. (16) Bryant CM, Dowell CJ, Fairbrother G. Caffeine reduction education to improve urinary symptoms. *Br J Nurs*. 2002;11(8):560-565. (17) Fantl JA, Wyman JF, McClish DK, et al. Efficacy of bladder training in older women with urinary incontinence. *JAMA*. 1991;265(5):609-613. (18) Subak LL, Quesenberry CP, Posner SF, Cattolica E, Soghikian K. The effect of behavioral therapy on urinary incontinence: a randomized controlled trial. *Obstet Gynecol*. 2002;100(1):72-78. (19) Van Kerrebroeck P, Kredet K, Jonas U, Zinner N, Wein A. Tolerodine once-daily: superior efficacy and tolerability in the treatment of the overactive bladder. *Urology*. 2001;57(3):414-421. (20) Nitti VW, Khullar V, van Kerrebroeck P, et al. Mirabegron for the treatment of overactive bladder: a prespecified pooled efficacy analysis and pooled safety analysis of three randomised, double-blind, placebo-controlled, phase III studies. *Int J Clin Pract*. 2013;67(7):619-632. (21) Burgio KL, Locher JL, Goode PS, et al. Behavioral vs drug treatment for urge urinary incontinence in older women: a randomized controlled trial. *JAMA*. 1998;280(23):1995-2000. (22) Breyer BN, Phelan S, Hogan PE, et al. Intensive lifestyle intervention reduces urinary incontinence in overweight/obese men with type 2 diabetes: results from the Look AHEAD trial. *J Urol*. 2014;192(1):144-149. (23) Burgio KL, Goode PS, Johnson TM, et al. Behavioral versus drug treatment for overactive bladder in men: the Male Overactive Bladder Treatment in Veterans (MOTIVE) Trial. *J Am Geriatr Soc*. 2011;59(12):2209-2216. (24) Kaplan SA, Roehrborn CG, Rovner ES, Carlsson M, Bavendam T, Guan Z. Tolerodine and tamsulosin for treatment of men with lower urinary tract symptoms and overactive bladder: a randomized controlled trial. *JAMA*. 2006;296(19):2319-2328.

About this publication

These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition. More detailed information on this topic is provided in a longer evidence document at alosafoundation.org.



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Medical writer: Stephen Braun.



Pharmaceutical Assistance
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Supplementary material 12. Examples of topic guides

The topic guide was iteratively refined as the study progressed to pursue emerging themes. Examples of topic guides 1 and 5 are presented below.

Topic guide 1

1. What were your initial thoughts when you heard about the academic detailing (AD)/educational visit being carried out in MPHC?
2. Have any of you any previous experience with academic detailing/educational visit before? If so how did it compare with the one delivered in MPHC?
3. What did you think of the process of organising the visit in MPHC?
4. What did you think of the topic delivered i.e. urinary incontinence (this topic was agreed with Dr Andrew Clare and Dr Tony Heffernan in advance of the visit)
5. How did you feel about this one on one interaction?
6. Do you think there was sufficient time allocated for the visit? Why?
7. What do you think of a pharmacist conducting these visits as opposed to other health care professionals?
8. How did you find the pharmacist's knowledge on the topic?
9. How did you find the pharmacist's ability to answer any of your questions on this topic?
10. What did you think of the printed material? I.e. was the content useful? Was it accurate and up to date?
11. What did you know at the end of the educational visit that you didn't know at the beginning of it? If anything?
12. Have you used any of the information discussed during the visit in the management of your incontinence patients? If so, how?
13. Do you think academic detailing/educational visit would impact on your management of patients with urinary incontinence? Can you visualise a case?
14. What would your response be if another educational visit was organised in the future?
15. Have you any further comments?

Topic guide 5

1. What were your initial thoughts when you heard about the educational visit being carried out in your practice?
2. Have any of you any previous experience with educational visits before? If so how did it compare with the one delivered in your practice?
3. What did you think of the topic delivered i.e. urinary incontinence (this topic was agreed with GPs in another practice)? Was it relevant?
4. What other topics do you think might be relevant?
5. How did you find this one on one educational interaction?
 - a. Do you think this style of interaction has advantages or disadvantages over routine educational types? If so, how?
6. Do you think there was sufficient time allocated for the visit? Some GPs mentioned the word brevity in relation to the visit.
7. If you had to explain to a colleague of yours what this educational visit is. What are the words that you'd use to describe it?
8. What do you think of a pharmacist conducting these visits as opposed to other health care professionals?
9. How did you find the pharmacist's knowledge on the topic?
10. What did you think of the printed material? I.e. was it relevant? Was it of good quality? What about the content?
 - a. Some GPs mentioned that it was visually appealing and easy to understand.
11. What did you know at the end of the educational visit that you didn't know at the beginning of it? If anything?
12. How effective do you think this type of educational visit is? Somebody sitting down with a GP for 10 or 15 minutes and going through the evidence relating to a clinical topic. Do you think that it would change your behaviour? How?
13. Is there anything that could be done differently to make the visit more beneficial for you?

- a. Some GPs had mentioned completing an assessment i.e. a series of MCQ's in their spare time after the educational visit was carried out to assess their knowledge.
 - b. Some GPs mentioned having an electronic form of the material on the computer desktop would allow it to be more readily accessible.
14. How could this type of educational visit be rolled out to other GP practices?
Do you think it is a practical program that can be delivered with GPs?
- a. Some GPs mentioned delivering it at CME meetings.
 - b. Some GPs suggested promoting it in a GP magazine i.e. Forum.
15. Some GPs had mentioned that the educational visit should have an academic input. What are your thoughts on that?
16. What would your response be if you were asked to participate in another educational visit?
17. Have you any further comments?

Supplementary material 13. GRAMMS framework.

The GRAMMS includes the following set of quality guidelines:

1. Describe the justification for using a mixed methods approach to the research question.

To date, no studies have evaluated the feasibility and acceptability of an academic detailing intervention with GPs in Ireland using mixed methods research. Therefore, the aim of this study was to assess the feasibility and acceptability of a pharmacist-led academic detailing intervention with a sample of practising GPs using a mixed methods approach.

2. Describe the design in terms of the purpose, priority and sequence of methods.

In this study a convergent parallel mixed method design was adopted as the qualitative and quantitative data were collected and analysed separately. Data were collected from the qualitative focus groups while quantitative data were collected from patient medical records (PMRs) on the GP practice database. The results of the qualitative and quantitative data analyses were then merged and interpreted.

3. Describe each method in terms of sampling, data collection and analysis.

Qualitative focus groups were conducted with GPs to explore the feasibility and acceptability of the intervention. This interview method was chosen due to its ability to generate data by interaction between group participants. Participants can present their own views and can listen to the contributions from others in the group. This allows additional material to be triggered in response to what is reported by others. There was also a shared background to the research topic among the GPs (urinary

incontinence). The descriptions of the GPs views were analysed using thematic analysis. This approach was used as it provides a flexible and useful research tool, which can potentially provide a rich and detailed account of the data. The medical records for all patients aged ≥ 65 years who were attending a participating GP with a diagnosis of urinary incontinence were retrieved and analysed using a before-after approach. Their medical records were analysed at multiple time points before and after the intervention (six and three months before the intervention (T_{-6}), (T_{-3}), at the time of the intervention (T_0) and three and six months after the intervention (T_3), (T_6). The following patient information were recorded for each patient: patient demographics, body measurements, chronic prescription medicines and medical history. The following criteria were then applied to the data:

- LUTS-FORTA criteria. These criteria were applied as they are the only criteria that review drugs to treat lower urinary tract symptoms.
- The Drug Burden Index (DBI). These criteria were applied as they measure the cumulative exposure to anticholinergic and sedative medicines in older people and its impact on physical and cognitive function.
- Anticholinergic cognitive burden scale (ACB). These criteria were applied to measure the cumulative effect of taking multiple medicines with anticholinergic properties.
- STOPP/START V2 criteria. Applying these criteria would capture how complicated these patients are in relation to their comorbidities and medicines prescribed.

4. Describe where integration has occurred, how it has occurred and who has participated in it.

This study used a mixed-methods approach to 1) qualitatively explore the feasibility and acceptability of an AD intervention among GPs in primary care and 2) quantitatively evaluate the ability of measuring an impact of the intervention. The integration of the qualitative and quantitative data occurred in the discussion section of the manuscript.

5. Describe any limitation of one method associated with the presence of the other method.

Combining and analysing the qualitative and quantitative approaches in the study was time consuming as equal weight had to be given to both sets of data.

6. Describe any insights gained from mixing or integrating methods.

The qualitative data supplemented the quantitative data by identifying convergence and divergence between the two datasets.

Supplementary material 14. Drugs identified by the LUTS-FORTA criteria

Drug class	Agent	FORTA class	Drugs identified by LUTS-FORTA in the study
5 α -reductase inhibitors	Dutasteride	B	√
	Finasteride	B	X
α_1 -blockers	Alfuzosin	D	X
	Doxazosin	D	X
	Sildosin	C	√
	Tamsulosin	C	√
	Terazosin	D	X
Antimuscarinics	Darifenacin	C	X
	Fesoterodine	B	√
	Oxybutynin standard dose/immediate release	D	√
	Oxybutynin low dose/extended release	C	√
	Propiverine	D	√
	Solifenacin	C	√
	Tolterodine	C	√
	Trospium	C	√
β_3 -agonist	Mirabegron	C	√
PDE5 inhibitor	Tadalafil	C	X

Supplementary material 15. STOPP/START V2 criteria applied to the data

Physiological system	Criteria	Criteria included	Number (%) of criteria included out of total criteria
	STOPP criteria		
Indication of medication	<p>A1. Any drug prescribed without an evidence-based clinical indication.</p> <p>A2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.</p> <p>A3. Any duplicate drug class prescription i.e. 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).</p>	<p>✓</p> <p>✓</p> <p>✓</p>	3/3 (100)
Cardiovascular system	<p>B1. Digoxin for heart failure with preserved systolic ventricular function (no clear evidence of benefit)</p> <p>B2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).</p> <p>B3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).</p> <p>B4. Beta blocker with symptomatic bradycardia (< 50/min), type II heart block or complete heart block (risk of profound hypotension, asystole).</p> <p>B5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)</p> <p>B6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).</p> <p>B7. 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).</p> <p>B8. 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).</p>	<p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>X</p> <p>X</p> <p>✓</p> <p>X</p>	7/13 (53.8)

	<p>B9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).</p> <p>B10. Centrally-acting antihypertensives (i.e. 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).</p> <p>B11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.</p> <p>B12. Aldosterone antagonists (i.e. spironolactone, eplerenone) with concurrent potassium-conserving drugs (i.e. 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).</p> <p>B13. Phosphodiesterase type-5 inhibitors (i.e. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent daily nitrate therapy for angina (risk of cardiovascular collapse).</p>	<p>✓</p> <p>X</p> <p>X</p> <p>X</p> <p>✓</p>	
Antiplatelet/Anticoagulant drugs	<p>C1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).</p> <p>C2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).</p> <p>C3. 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).</p> <p>C4. 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)</p>	<p>✓</p> <p>✓</p> <p>✓</p> <p>X</p>	8/11 (72.7)
	<p>C5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation without a clear indication for aspirin (no added benefit from aspirin).</p> <p>C6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease without a clear indication for anticoagulant therapy (no added benefit from dual therapy).</p>	<p>✓</p> <p>✓</p>	

	<p>C7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).</p> <p>C8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (i.e. thrombophilia) for > 6 months, (no proven added benefit).</p> <p>C9. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (i.e. thrombophilia) for > 12 months (no proven added benefit).</p> <p>C10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of gastrointestinal bleeding).</p> <p>C11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease).</p>	<p>✓</p> <p>X</p> <p>X</p> <p>✓</p> <p>✓</p>	
CNS & Psychotropic drugs	<p>D1. Tricyclic antidepressants with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).</p> <p>D2. Initiation of tricyclic antidepressants as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).</p> <p>D3. Neuroleptics with moderate-marked antimuscarinic/anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenazine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).</p> <p>D4. 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).</p> <p>D5. 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 > 2 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).</p> <p>D6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms).</p> <p>D7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity).</p> <p>D8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).</p>	<p>✓</p> <p>X</p> <p>✓</p> <p>X</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p>	10/14 (71.4)

	<p>D9. 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).</p> <p>D10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).</p> <p>D11. 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).</p> <p>D12. 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).</p> <p>D13. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy).</p> <p>D14. First-generation antihistamines (safer, less toxic antihistamines now widely available).</p>	<p>X</p> <p>✓</p> <p>✓</p> <p>X</p> <p>✓</p> <p>✓</p>	
Renal system	<p>E1. 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).</p> <p>E2. Direct thrombin inhibitors (i.e. dabigatran) if eGFR < 30 ml/min/1.73m² (risk of bleeding).</p> <p>E3. Factor Xa inhibitors (i.e. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m² (risk of bleeding).</p> <p>E4. NSAID's if eGFR < 50 ml/min/1.73m² (risk of deterioration in renal function).</p> <p>E5. Colchicine if eGFR < 10 ml/min/1.73m² (risk of colchicine toxicity).</p> <p>E6. Metformin if eGFR < 30 ml/min/1.73m² (risk of lactic acidosis).</p>	<p>X</p> <p>X</p> <p>X</p> <p>X</p> <p>X</p> <p>X</p>	0/6 (0)
Gastrointestinal system	<p>F1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).</p> <p>F2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).</p>	<p>✓</p> <p>✓</p>	4/4 (100)

	<p>F3. Drugs likely to cause constipation (i.e. 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).</p> <p>F4. Oral elemental iron doses greater than 200 mg daily (i.e. ferrous fumarate > 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate > 1800 mg/day; no evidence of enhanced iron absorption above these doses).</p>	<p>✓</p> <p>✓</p>	
Respiratory system	<p>G1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).</p> <p>G2. 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).</p> <p>G3. Antimuscarinic bronchodilators (i.e. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention).</p> <p>G4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).</p> <p>G5. Benzodiazepines with acute or chronic respiratory failure i.e. $pO_2 < 8.0 \text{ kPa} \pm pCO_2 > 6.5 \text{ kPa}$ (risk of exacerbation of respiratory failure).</p>	<p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>X</p>	4/5 (80)
Musculoskeletal system	<p>H1. 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).</p> <p>H2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).</p> <p>H3. 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).</p> <p>H4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis (risk of systemic corticosteroid side-effects).</p> <p>H5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).</p>	<p>✓</p> <p>✓</p> <p>X</p> <p>✓</p> <p>✓</p>	8/9 (88.9)

	<p>H6. Long-term NSAID or colchicine (> 3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor i.e. allopurinol, febuxostat (xanthine-oxidase inhibitors are first choice prophylactic drugs in gout).</p> <p>H7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke).</p> <p>H8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease).</p> <p>H9. 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).</p>	<p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p>	
Urogenital system	<p>I1. 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).</p> <p>I2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)</p>	<p>✓</p> <p>✓</p>	2/2 (100)
Endocrine system	<p>J1. Sulphonylureas with a long duration of action (i.e. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).</p> <p>J2. Thiazolidinediones (i.e. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure).</p> <p>J3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).</p> <p>J4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).</p> <p>J5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).</p> <p>J6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of hypogonadism indication).</p>	<p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p>	6/6 (100)
Drugs that predictably increase the risk of falls in older people	<p>K1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).</p> <p>K2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).</p> <p>K3. Vasodilator drugs (i.e. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers, diazoxide, minoxidil, hydralazine) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure \geq 20mmHg (risk of syncope, falls).</p>	<p>✓</p> <p>✓</p> <p>X</p>	3/4 (75)

	K4. Hypnotic Z-drugs i.e. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).	✓	
Analgesic drugs	L1. 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).	X	2/3 (66.7)
	L2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation).	✓	
	L3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain).	✓	
Antimuscarinic/Anticholinergic drug burden	N. Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties (i.e. bladder antispasmodics, intestinal antispasmodics, tricyclic antidepressants, first generation antihistamines) (risk of increased antimuscarinic/anticholinergic toxicity).	✓	1/1 (100)
Total STOPP criteria n=80			58/80 (72.5)
	START criteria		
Cardiovascular system	A1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.	✓	7/8 (87.5)
	A2. 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.	✓	
	A3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.	✓	
	A4. 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.	X	
	A5. 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.	✓	
	A6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.	✓	
	A7. Beta-blocker with ischaemic heart disease.	✓	
	A8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprololorcarvedilol) with stable systolic heart failure.	✓	

Respiratory system	B1. Regular inhaled beta 2 agonist or antimuscarinic bronchodilator (i.e. ipratropium, tiotropium) for mild to moderate asthma or COPD.	✓	1/3 (33.3)
	B2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids.	X	
	B3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%).	X	
Central nervous system & Eyes	C1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability.	✓	3/6 (50)
	C2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.	X	
	C3. Acetylcholinesterase inhibitor (i.e. donepezil, rivastigmine, galantamine) for mild-moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).	✓	
	C4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.	✓	
	C5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.	X	
	C6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.	X	
Gastrointestinal system	D1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.	✓	2/2 (100)
	D2. Fibre supplements (i.e. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation.	✓	
Musculoskeletal system	E1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.	✓	7/7 (100)
	E2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.	✓	
	E3. 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).	✓	
	E4. Bone anti-resorptive or anabolic therapy (i.e. 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).	✓	

	E5. 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).	✓	
	E6. Xanthine-oxidase inhibitors (i.e. allopurinol, febuxostat) with a history of recurrent episodes of gout.	✓	
	E7. Folic acid supplement in patients taking methotexate.	✓	
Endocrine system	F1. ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. overt dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment.	X	0/1 (0)
Urogenital system	G1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary.	X	1/3 (33.3)
	G2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary.	X	
	G3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.	✓	
Analgesics	H1. 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.	X	1/2 (50)
	H2. Laxatives in patients receiving opioids regularly.	✓	
Vaccines	I1: Seasonal trivalent influenza vaccine annually.	X	0/2 (0)
	I2: Pneumococcal vaccine every 5 years, according to national guidelines.	X	
Total START criteria n=34			22/34 (64.7)

Appendix V. Supplementary material for Chapter 7.

Supplementary material 16. FORUM article.

News

Academic detailing initiative for primary care prescribers

Academic detailing is an interactive educational outreach service to prescribers in primary and long-term care settings to provide unbiased, non-commercial, evidence-based information about medications and other therapeutic decisions, with the goal of improving patient care.

This service which is free to users, is usually provided to prescribers one-on-one in their own practice with visits scheduled in advance. Each educational session is tailored to the needs of the individual prescriber and the specific clinical areas they would like to focus on.

Educational materials that are provided during the visit are evidence-based with appropriate referencing. Information highlighted to prescribers often includes recommendations about alternative treatment regimens or non-pharmacological interventions where appropriate.

These recommendations are designed to complement the clinical judgement of a prescriber and not to

replace it. This evidence-based strategy has been shown to be an effective means of changing prescribing behaviour and improving patient care.

While academic detailing has been adopted in other countries, this strategy is not routinely available in Irish general practice. However, an academic detailing feasibility study was recently delivered to a number of GPs in the Cork area.

This study involved a pharmacist delivering an educational session on the topic of urinary incontinence to GPs in their practice. The effectiveness of this educational service is currently being evaluated and depending on the findings of the study it may be rolled out to GPs nationally.

This study is being funded by SPHeRE (Structured Population and Health-services Research Education) and the HRB (Health Research Board). If you would like to know more about academic detailing please contact, Email: davidorjordan@ucc.ie or Tel: 021-4901690.

New book to improve understanding of migraine

A new book *Migraine – Not Just another Headache* has just been published

and describes migraine in detail, its diagnosis, impact, trends, triggers, treatment and the lived experiences of those who suffer migraines in their everyday lives.

The book is edited by clinical psychologist Dr Marie Murray in collaboration with the Migraine Association of Ireland. It includes chapters on various aspects of migraine written by experts, including Dr Murray, Dr Orla Hardiman and Dr Eddie O'Sullivan.

Migraine – Not Just another Headache is published by Curach Press and available online from www.migraine.ie and also available in store at Easons and other independent bookshops.



Three-day meeting on primary care dermatology

The Primary Care Dermatology Society of Ireland (PCDSI) is holding its 21st three-day conference from Thursday, March 30 to Saturday, April 1 in the Killashee House Hotel, Co Kildare.

This year's programme includes a full study day in dermoscopy on the Thursday. Four high calibre experts in dermoscopy will run joint sessions both at basic level for those introducing themselves to dermoscopy and also an advanced grouping for those who wish to refresh their skills and expand their knowledge of the more challenging aspects of dermoscopy. On Friday and Saturday there is a packed two-day programme of general dermatology topics.

The Society says it is always keen to welcome new members and attendees who wish to develop an interest in dermatology or enhance their existing knowledge for the 10% plus of consultations in general practice that involve a skin presentation. For those interested in attending some or part of this educational meeting, registration and programme details are available on www.pcdsi.com



The International Advisory Committee meeting of the HRB Primary Care Clinical Trials Network Ireland (HRB PC CTNI) took place recently in Galway. The HRB PC CTNI was established in July 2015 and is funded for five years by the HRB. Pictured above are (l-r): Prof Brendan Delaney (Imperial College London), Edel Murphy (HRB PC CTNI), Prof Susan Smith (RCSI), Dr Paul O'Connor (HRB PC CTNI), Dr Molly Byrne (NUI Galway), Prof Bruce Guthrie (Scottish PCRN), Prof Andrew Murphy (HRB PC CTNI), Dr Claire Collins (ICGPI), Professor Margaret Cupples (Queen's University Belfast), Dr Akke Vellings (HRB PC CTNI), Professor Frank Sullivan (University of Toronto), Dr Paddy Gillespie (NUI Galway), Prof Declan Devane (NUI Galway), Brada Kelleher (HRB PC CTNI) and Prof Eva Hummer-Pradler, Göttingen University, Germany



The Resistant Hypertension Study Advisory Committee (HRB three-year funded study based in general practice, NUI Galway) met in Galway recently. Pictured left are (sitting): Prof Eoin O'Brien (UCD), Hannah Dunand (NUIG) and Brendan Harman (NUIG); and standing: Dr Peter Hayes (NUIG), Monica Casey (NUIG), Prof Roman O'Carroll (University of Stirling), Prof Andrew Murphy (NUIG), Dr Eamon Dolan (RCSI) and Dr Gerry Molloy (NUIG)

Appendix VI. Education and training undertaken during the PhD

Date	Education and training
October 2013- September 2015	<p>SPHeRE Scholars Programme in Health Services Research. The following modules were undertaken:</p> <ul style="list-style-type: none"> • EH7003: Evidence Synthesis and Clinical Trials (5 credits). • EH7005: Introduction to Health Economics and Econometrics (10 credits). • EH7009: Population and Individual Health (10 credits). • EH7010: Health Systems, Policy and Informatics (10 credits). • EH7011: Integrated Epidemiology/Biostatistics (10 credits). • EH7014: National work placement: 8 week placement with the TRUST trial (5 credits). • OH7013: Quantitative and Qualitative Research Methods (10 credits). • PG7016: Systematic Reviews for the Health Sciences (5 credits). • EH7012: Research Development and Academic writing (5 credits). • EH7013: International placement: 4 week placement at Inselspital, Bern University Hospital, Switzerland (5 credits).
May 2014	<ul style="list-style-type: none"> • Presentation skills, Irish Times training, Royal College of Surgeons Ireland (RCSI).
May 2014	<ul style="list-style-type: none"> • The importance of academic feedback, Dr Carlos Bruen, RCSI.
May 2014	<ul style="list-style-type: none"> • Research prioritisation and impact, Dr Carlos Bruen, RCSI.
October 2014	<ul style="list-style-type: none"> • Completing ethics applications, Professor Anne Hickey, RCSI.
October 2014	<ul style="list-style-type: none"> • Research troubleshooting, Professor Anne Hickey, RCSI.
November 2014	<ul style="list-style-type: none"> • NVivo 2 day Training Course, Mr Ben Meehan, University College Cork.
February 2015	<ul style="list-style-type: none"> • What Contribution will your PhD make? Dr Sarah Barry, Dr Niamh Humphries, RCSI.
February 2015	<ul style="list-style-type: none"> • Introduction to analysing qualitative interviews, Health Experiences Research Group at the University of Oxford.
March 2015	<ul style="list-style-type: none"> • Code of good practice, Dr Niamh Humphries, RCSI.
April 2015	<ul style="list-style-type: none"> • Writing skills, Professor Ivan Perry, UCC.
April 2015	<ul style="list-style-type: none"> • Behaviour change interventions, Dr Molly Byrne, RCSI.

Date	Education and training
April 2015	<ul style="list-style-type: none"> Qualitative troubleshooting, Dr Sarah Barry, RCSI.
November 2015	<ul style="list-style-type: none"> Publishing in a peer review journal, Dr Trish Groves, Head of Research, BMJ & Editor-in-chief, BMJ Open, UCC.
January 2016	<ul style="list-style-type: none"> Getting research into policy, Professor Ruairi Brugha, RCSI.
March 2016	<ul style="list-style-type: none"> Leadership, Professor Patricia Kearney, RCSI.
March 2016	<ul style="list-style-type: none"> Grant writing, Professor Kathleen Bennett, RCSI.
March 2016	<ul style="list-style-type: none"> Managing a career in Population Health and Health Services Research (PHHSR), Dr Eithne Sexton, Dr Lisa Mellon, Dr Niamh Humphries, Dr Richard Layte, RCSI.
May 2016	<ul style="list-style-type: none"> Academic detailing (AD) training workshop, National Resource Center for Academic Detailing (NARCAD) in Boston, USA.
March 2017	<ul style="list-style-type: none"> Communicating your research for policy, Dr Carlos Bruen, Dr Sara McAleese, Dr Conor Keegan, RCSI.

Appendix VII. Ethics



UCC

DOR

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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.

26th March 2015

Our ref: ECM 3 (mmm) 14/04/15 & 4 (k) 07/10/14

Professor Stephen Byrne
Professor of Clinical Pharmacy
Cavanagh Pharmacy Building
College Road
Cork

Re: Optimising prescribing practices in community dwelling older adults.

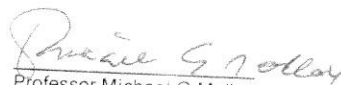
Dear Professor Byrne

The Chairman approved the following:

- Amendment Application Form
- Inclusion of GP's in Cork and Kerry area.

Full approval is granted to implement this amendment.

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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University College Cork, Ireland

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Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (j) 07/07/15

21st May 2015

Dr Stephen Byrne
Senior Lecturer in Clinical Pharmacy
University College Cork
Room 2.02
Cavanagh Pharmacy Building
College Road
Cork

Re: Quasi-experimental study investigating the impact of a pharmacist led medication screening tool for use in primary care.

Dear Dr Byrne

The Chairman approved the following:

- Amendment Application Form
- Change in co-investigator from Mr Richard O'Sullivan to Mr David O'Riordan.

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



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University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

10th June 2016

Our ref: ECM 4 (s) 10/05/16 & ECM 3 (qqqq) 21/06/16

Professor Stephen Byrne
School of Pharmacy
University College Cork
Room 1.02
Cavanagh Pharmacy Building
College Road
Cork

Re: A feasibility study of an educational outreach visit with GPs in Primary Care.

Dear Professor Byrne

The Chairman approved the following:

- Revised Invitation Letter
- Revised Consent Form.

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 Hospital

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10th September 2014

Our ref: ECM 4 (k) 07/10/14

Professor Stephen Byrne
Professor of Clinical Pharmacy
Cavanagh Pharmacy Building
College Road
Cork

Re: Optimising prescribing practices in community dwelling older adults.

Dear Professor Byrne

Expedited approval will be granted to carry out the above study at:

- Mallow Primary Health Centre

subject to receipt of the following:

- STOPP/START Screening Tool
- Information Sheet and Consent Form for Interview
- Interview Questions.

The following document has been approved:

- Application Form.

The co-investigators involved in this study will be:

- Mr David O'Riordan, Professor Patricia Kearney and Dr Carol Sinnott.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

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Ollscoil na hÉireann, Corcaigh - National University of Ireland, Cork



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1st October 2014

Our ref: ECM 3 (ggggg) 07/10/14

Professor Stephen Byrne
Professor of Clinical Pharmacy
Cavanagh Pharmacy Building
College Road
Cork

Re: Optimising prescribing practices in community dwelling older adults.

Dear Professor Byrne

The Chairman approved the following:

- STOPP/START Screening Tool
- Information Sheet and Consent Form for Interview
- Interview Questions.

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

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Ollscoil na hÉireann, Corcaigh, Mionteacht Ollscoile, Corcaigh, Éire



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24th February 2017

Our ref: ECM 4 (s) 10/05/16 & ECM 3 (ddddd) 07/03/17

Professor Stephen Byrne
School of Pharmacy
University College Cork
Room 1.02
Cavanagh Pharmacy Building
College Road
Cork

Re: A feasibility study of an educational outreach visit with GPs in Primary Care.

Dear Professor Byrne

The Chairman approved the following:

- Cover Letter dated 13th February 2017
- Amendment Application Form signed 13th February 2017
- Study Plan Version 2b dated 13th February 2017.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospital

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