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Rationalising Antipsychotic Prescribing in Dementia: A Mixed-Methods Investigation

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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

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List of Abbreviations

AAIC	Alzheimer's Association International Conference
ABC	Antecedent-Behaviour-Consequence
ACOVE	Assessing Care of Vulnerable Elders
AD	Alzheimer's Disease
ADR	Adverse Drug Reaction
aOR	Adjusted Odds Ratio
AOU	Assessment of Underutilisation of Medication
APEASE	Acceptability, Practicability, Effectiveness/cost-effectiveness, Affordability, Safety/side-effects, Equity
APID	Appropriate Psychotropic drug use In Dementia
ASI	Alzheimer Society of Ireland
ATC	Anatomical Therapeutic Chemical
BCT	Behaviour Change Technique
BCTTv1	Behaviour Change Technique Taxonomy version 1
BCW	Behaviour Change Wheel
BI	Barthel Index
BPSD	Behavioural and Psychological Symptoms of Dementia
CARDI	Centre for Ageing Research and Development in Ireland
CASP	Critical Appraisal Skills Programme
CERQual	Confidence in the Evidence from Reviews of Qualitative Research
CI	Confidence Interval
CICI	Context and Implementation of Complex Interventions
CME	Continuing Medical Education
CMS	Centres for Medicare and Medicaid Services
CNM	Clinical Nurse Manager
COM-B	Capabilities Opportunities Motivation – Behaviour

COS	Core Outcome Set
COREQ	COnsolidated criteria for REporting Qualitative research
CPD	Continuing Professional Development
CPZ	Chlorpromazine
CREC	Clinical Research Ethics Committee
CRPD	Convention on the Rights of Persons with Disabilities
DLB	Dementia with Lewy Bodies
DNNI	Dementia and Neurodegeneration Network of Ireland
ED	Emergency Department
EMA	European Medicines Agency
ENTREQ	ENhancing Transparency in REporting the synthesis of Qualitative research
EQUATOR	Enhancing the QUAlity and Transparency Of health Research
EU	European Union
FDA	Food and Drug Administration
FTD	Frontotemporal Dementia
GP	General Practitioner
GRAMMS	Good Reporting of a Mixed Methods Study
GRIPP2-SF	Guidance for Reporting Involvement of Patients and the Public - Short Form
HALT	Halting Antipsychotic use in Long-Term care
HCA	Healthcare assistant
HIQA	Health Information and Quality Authority
HPRA	Health Products Regulatory Authority
HSE	Health Services Executive
HSRPP	Health Services Research and Pharmacy Practice
IAGG	International Association of Gerontology and Geriatrics
ICGP	Irish College for General Practitioners
ICPE	International Conference on Pharmacoepidemiology and Therapeutic Risk Management

IGS	Irish Gerontological Society
INAD	Irish National Audit of Dementia Care
IPU	Irish Pharmacy Union
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
IQR	Interquartile Range
LBD	Lewy Body Dementia
LPN	Licensed Practical Nurse
LTC	Long-Term Care
MAI	Medication Appropriateness Index
MBI	Mild Behavioural Impairment
MCI	Mild Cognitive Impairment
MRC	Medical Research Council
NIHR	National Institute for Health Research
NNH	Number Needed to Harm
NPI-NH	Neuropsychiatric Inventory-Nursing Home
NPS	Neuropsychiatric Symptoms
NRCT	Non-Randomised Controlled Trial
OBRA	Omnibus Budget Reconciliation Act
OD	Occupational Disruptiveness
PCRS	Primary Care Reimbursement Service
PDD	Parkinson's Disease Dementia
PICO	Population Intervention Comparator Outcome
PIM	Potentially Inappropriate Medication
PINCH-ME	Pain Infection Nutrition Constipation Hydration Medication Environment
PIP	Potentially Inappropriate Prescribing
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRIMM	Prescribing and Research in Medicines Management

PRN	*Pro Re Nata*
PwD	People/Person with Dementia
QUM-D	Quality Use of Medications in Dementia
RAPID	Rationalising Antipsychotic Prescribing In Dementia
RASP	Rationalisation of home medication by an Adjusted STOPP list in older Patients
RCT	Randomised Controlled Trial
RedUSe	Reducing Use of Sedatives
RN	Registered Nurse
RR	Relative Risk
SCU	Specialist Care Unit
SD	Standard Deviation
SMMSE	Standardised Mini-Mental State Examination
SPHeRE	Structured Population and Health-Services Research Education
START	Screening Tool to Alert doctors to Right Treatment
STOPP	Screening Tool of Older Person's Prescriptions
STROBE	Strengthening The Reporting of OBservational studies in Epidemiology
TDF	Theoretical Domains Framework
TIDieR	Template for Intervention Description and Replication
UK	United Kingdom
UN	United Nations
US	United States
VaD	Vascular Dementia
WHELD	Wellbeing and HEaLth for people with Dementia
WHO	World Health Organisation

Declaration

This is to certify that the work I am submitting is my own and has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism.

Signed: _____ Date: _____

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Publications and Presentations

Thesis Related Publications

1. 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 Jan 10; 45(2):201-9. (1) (Chapter 2)
   https://www.ncbi.nlm.nih.gov/pubmed/26755524
2. Walsh KA, O'Regan NA, Byrne S, Browne J, Meagher DJ, Timmons S. Patterns of psychotropic prescribing and polypharmacy in older hospitalized patients in Ireland: the influence of dementia on prescribing. International Psychogeriatrics. 2016 Nov; 28(11):1807-20. (2) (Chapter 3)
   https://www.ncbi.nlm.nih.gov/pubmed/27527842
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4. Walsh KA, Sinnott C, Fleming A, Mc Sharry J, Byrne S, Browne J, Timmons S. Exploring Antipsychotic Prescribing Behaviors for Nursing Home Residents With Dementia: A Qualitative Study. Journal of the American Medical Directors Association. 2018 Nov 1;19(11):948-58. (4) (Chapter 5)

https://www.ncbi.nlm.nih.gov/pubmed/30241987

Non-thesis Related Publication

1. Stott DJ, Rodondi N, Kearney PM, Ford I, Westendorp RG, Mooijaart SP, Sattar N, Aubert CE, Aujesky D, Bauer DC, Baumgartner C. *et al.* Thyroid hormone therapy for older adults with subclinical hypothyroidism. New England Journal of Medicine. 2017 Jun 29;376(26):2534-44. (5)
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systematic review and meta-ethnography. Systematic reviews. 2018 Dec;7(1):62. (8)

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6. O'Riordan D, Aubert CE, Walsh KA, Van Dorland A, Rodondi N, Du Puy RS, Poortvliet RK, Gussekloo J, Sinnott C, Byrne S, Galvin R. Prevalence of potentially inappropriate prescribing in a subpopulation of older European clinical trial participants: a cross-sectional study. BMJ open. 2018 Mar 1;8(3):e019003. (10)

   https://www.ncbi.nlm.nih.gov/pubmed/29567842

Thesis Related Presentations

1. Improving the appropriateness of prescribing in older patients: a systematic review and meta-analysis of pharmacists' interventions in secondary care.
   - Health Services Research and Pharmacy Practice (HSRPP) Conference, 2015. Belfast (Oral Presentation)
   - International Association of Gerontology and Geriatrics (IAGG) Conference, 2015. Dublin (Poster Presentation)
   - All Ireland Pharmacy Conference, 2015. Dundalk (Poster Presentation)

2. Patterns of psychotropic prescribing and polypharmacy in older hospitalized patients in Ireland: the influence of dementia on prescribing.
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    - Structured Population and Health Services Research Education (SPHeRE) Network Conference, 2016. Dublin (Oral Presentation)
    - Prescribing and Research in Medicines Management (PRIMM), 2016. London (Poster Presentation)
3. Influences on Decision-Making Regarding Antipsychotic Prescribing in Nursing Home Residents With Dementia: A Systematic Review and Synthesis of Qualitative Evidence.
    - New Horizons Conference, 2016. Cork (Poster Presentation)
    - Annual Nursing & Midwifery Research Conference 2016. Cork (Poster Presentation)
    - SPHeRE Conference, 2017. Dublin (Oral Presentation)
    - All Ireland Schools of Pharmacy Research Seminar, 2017. Cork (Poster Presentation)
    - Psychology, Health and Medicine, 2017. Dublin (Poster Presentation)
    - Alzheimer's Association International Conference (AAIC), 2017. London (Poster Presentation)
4. Exploring Antipsychotic Prescribing Behaviors for Nursing Home Residents With Dementia: A Qualitative Study.

- Irish Gerontological Society (IGS), Annual and Scientific Meeting, 2017. Wexford (Oral Presentation)

5. 'Thesis-in-3'
    - Dementia and Neurodegeneration Network of Ireland (DNNI) Conference, 2017. Dublin (Oral Presentation)
6. Development of the *'Rationalising Antipsychotic Prescribing in Dementia'* (RAPID) Complex Intervention using the Behaviour Change Wheel, with Patient and Public Involvement
    - SPHeRE Conference, 2018. Dublin (Poster Presentation)
    - HSRPP Conference, 2018. Newcastle (Oral Presentation)
7. The *'Rationalising Antipsychotic Prescribing in Dementia'* (RAPID) Complex Intervention: A Mixed-Methods Feasibility Study
    - Alzheimer Europe, 2018. Barcelona (Poster Presentation)

Non-thesis Related Presentations

1. 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.
    - International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE), 2016. Dublin (Poster Presentation)
2. Building Responsible Research and Innovation Proficiency through a Community-Based Participatory Research Module
    - Living Knowledge Conference, 2016. Dublin (Poster Presentation)

Thesis Abstract

Introduction

Antipsychotics are commonly prescribed to people with dementia, especially in nursing homes, despite limited benefits and significant harms. There have been calls to better understand the reasons why antipsychotics continue to be inappropriately prescribed to people with dementia, and to develop sustainable interventions. Hence the overarching aim of this thesis was to develop and assess the feasibility of a theoretically-informed, evidence-based and sustainable intervention to rationalise (or optimise) antipsychotic prescribing in nursing home residents with dementia.

Methods

The overarching Medical Research Council (MRC) framework for developing and evaluating complex interventions guided our approach to this mixed-methods research. Firstly, a systematic review was undertaken to determine the effectiveness of pharmacists' intervention in improving the appropriateness of prescribing in hospitalised older adults, with a particular focus on people with dementia. Secondly, a retrospective cross-sectional study was conducted examining prescribing differences between older adults with and without dementia, on admission to hospital. Next, a systematic review of qualitative evidence was undertaken to explore the influences on decision-making regarding antipsychotic prescribing in nursing home residents with dementia, which subsequently informed a semi-structured interview study exploring antipsychotic prescribing behaviours. The Behaviour

Change Wheel (BCW) was then used to develop a complex intervention with Patient and Public Involvement (PPI) throughout. Finally, a feasibility study of the novel intervention was conducted in a nursing home setting.

Results

Despite the fact that our cross-sectional study showed that hospitalised adults with dementia were prescribed significantly more antipsychotics, our systematic review found no pharmacist intervention existed which aimed to improve the quality of prescribing in this population. Our qualitative synthesis highlighted the complexity of decision-making with regards antipsychotic prescribing to nursing home residents with dementia. The interview study identified determinants influencing prescribing behaviours. Based on these findings, we developed the '*Rationalising Antipsychotic Prescribing in Dementia'* (RAPID) complex intervention which consisted of academic detailing with general practitioners, education and training with nursing home staff, and an assessment tool. This intervention was found to be both feasible and acceptable, however limited uptake of the assessment tool compromised intervention implementation.

Conclusion

This thesis has made a significant original contribution to knowledge, generating a much needed conceptual understanding of this complex issue and contributing towards intervention development. Further research is required to evaluate the effectiveness and sustainability of our novel intervention through larger scale evaluations.

Chapter 1. Introduction

1.1 Chapter Description

This chapter provides an overview of the literature and methodological approach which have informed my research. I begin by discussing Dementia: the various subtypes, the epidemiology, as well as the economic and societal impact. Secondly, I explain the prevalence, causes, impact and management of Behavioural and Psychological Symptoms of Dementia (BPSD). Following this, I discuss potentially inappropriate prescribing (PIP) in people with dementia, focusing specifically on antipsychotics. I define what is meant by *'off-label'* prescribing of antipsychotics in dementia; examining the prevalence rates across different settings and countries; and discussing the evidence of harms and benefits. Next, I focus on the evolving dementia policy landscape, the Health Information and Quality Authority (HIQA) and the impact of national approaches on antipsychotic prescribing. Then I briefly describe existing interventions to improve the appropriateness of prescribing to people with dementia. Finally, I present the aim and objectives; overarching methodological framework; the underpinning research paradigm; the study design; and the outline for the remainder of my thesis.

1.2 Dementia

1.2.1 What is Dementia?

Dementia is defined as a clinical syndrome, of a chronic and progressive nature, caused by neurodegeneration, in which there are difficulties with memory, language, problem-solving and other cognitive skills affecting a person's ability to perform everyday activities (11-13). Both cognitive (e.g. memory impairment) and non-cognitive problems (e.g. agitation and aggression) are core features of dementia (11, 14, 15). Dementia is generally considered to be an umbrella term to describe a group of diseases that cause these symptoms (16). Although age is the main risk factor for developing dementia with almost 95% of all those affected 65 years or older (13), it is important to acknowledge that it is not part of normal ageing (15).

1.2.2 The Main Causes (Subtypes) of Dementia and Clinical Presentations

There are many different causes, or subtypes, of dementia with Alzheimer's Disease (AD), being the most common, accounting for approximately 60-80% of all cases of dementia (11). The characteristic features of AD are the progressive accumulation of twisted strands of the protein tau (*tangles*) inside neurons in the brain and the protein fragment beta-amyloid (*plaques*) outside neurons (11). AD manifests in the early stages of those affected as difficulty remembering recent events, apathy and depression. Later symptoms include impaired communication, disorientation, confusion, poor judgment, distressing behaviours (e.g. agitation) and symptoms (e.g.

hallucinations) and ultimately, difficulty speaking, swallowing and independently mobilising (11).

Vascular dementia (VaD) in isolation accounts for approximately 10% of cases and is generally caused by cerebrovascular disease (11, 17). However VaD is more commonly found as a Mixed Dementia alongside AD, in up to approximately 50% of all cases of dementia with an Alzheimer's pathology (11, 18). In the early stages, VaD is characterised by an impaired ability to make decisions, plan or organise as opposed to the memory loss often associated with AD. Additionally, people with VaD can have significant difficulty with motor function (11).

Lewy Body Dementia (LBD) is another cause of dementia, and is usually classified as either Dementia with Lewy Bodies (DLB) or Parkinson's Disease Dementia (PDD) (19). LBD is associated with abnormal deposits of a protein called alpha-synuclein in the brain (11, 20). In DLB, parkinsonism (i.e. movement problems such as tremors, slow movement and stiffness) arises concurrently with or after the onset of dementia. Whereas, PDD is diagnosed when dementia occurs at least one year after the onset of Parkinson's disease (19). People with LBD commonly experience issues with attention, visuospatial activity and executive function. Visual hallucinations, gait imbalance, sleep disturbances and fluctuations in cognition are also particularly common in this cohort (19). DLB accounts for approximately 15% of cases of dementia, whereas PDD accounts for 3-5% of cases (14, 19).

Frontotemporal Dementia (FTD) tends to occur in younger people with dementia and has a stronger genetic component than other dementias (21). Early symptoms of FTD include impulsive or inappropriate behaviours (e.g. sexual disinhibition) and

difficulties with communication (aphasia), which can progress to more severe behaviours and ultimately an inability to communicate (21). These clinical manifestations occur as a result of disease in the frontal and/or temporal lobes of the brain which are responsible for executive decision-making, impulse control and language comprehension (21). FTD accounts for approximately 3% of all dementia cases, but is the most common type of dementia in men under the age of 55 (12, 22).

Other types of dementia which are less common include Creutzfeldt - Jakob Disease, Normal Pressure Hydrocephalus, Korsakoff's Disease, Huntington's Disease and HIV-Associated Dementia. Collectively, these rarer types of dementia account for about 8% of all dementia cases (23, 24).

For the remainder of this thesis, unless there is a need to specify the subtype of dementia, the term '*person with dementia*' shall be used to refer to a person with any subtype of dementia.

1.2.3 Epidemiology of Dementia

It is estimated that there are currently 50 million people living with dementia worldwide (25, 26). The global prevalence of dementia (50 million) is expected to increase to 82 million by 2030 and to 152 million by 2050 (26). To illustrate this dramatic increase in the prevalence of dementia globally, it is currently estimated that every three seconds, one new case of dementia is diagnosed (25). This rapid projected increase in the global prevalence of dementia is largely attributed to rising life expectancies worldwide and hence an ageing population (25).

In Ireland, an estimated 55,000 people are currently living with dementia, and this figure is projected to reach 132,000 by 2041 and 152,000 by 2046 (27). Approximately 63% of all those with dementia in Ireland are living in the community, while 34% reside in nursing home settings. The remaining 3% of people with dementia are located in acute or psychiatric settings (28).

1.2.4 The Economic and Societal Impact of Dementia

The long duration of illness before death, and the substantial level of comorbidity, contributes significantly to the economic and societal impact of dementia (11). Globally, dementia is now estimated to cost US$1 trillion, and this is projected to double to US$2 trillion by 2030 (25). In the United Kingdom (UK), dementia currently has higher health and social care costs (£11.9 billion) than heart disease (£2.5 billion) and cancer (£5.0 billion) combined (29). In Ireland, the total annual cost of dementia was estimated to be €1.69 billion in 2010 (28).

The economic cost of dementia is not evenly distributed between healthcare (costs to the health service due to hospitalisation and medication), social care (costs due to nursing home care, respite care and home care) and informal care (costs to family and friends providing unpaid care), with informal care providers bearing the greatest cost burden (28, 30). In Ireland, it was estimated that in 2010, €0.8 billion of the total economic cost of dementia was attributable to informal care (47%), whereas €0.73 billion was attributable to social (residential) care (43%) (28). Furthermore, the cost of dementia differs based on the severity of the disease and the care setting**. Figure 1** which is based on UK data, illustrates the breakdown of the estimated costs by residence and dementia severity per person. This graph shows us that the burden of

costs shifts from informal care to social care as a person with dementia moves into a nursing home setting (30). However as the prevalence of dementia is projected to increase dramatically over the next few decades (25), informal carers and social care systems in particular are both expected to face significant pressure to provide appropriate levels of care (**Figure 2**) (28, 30).

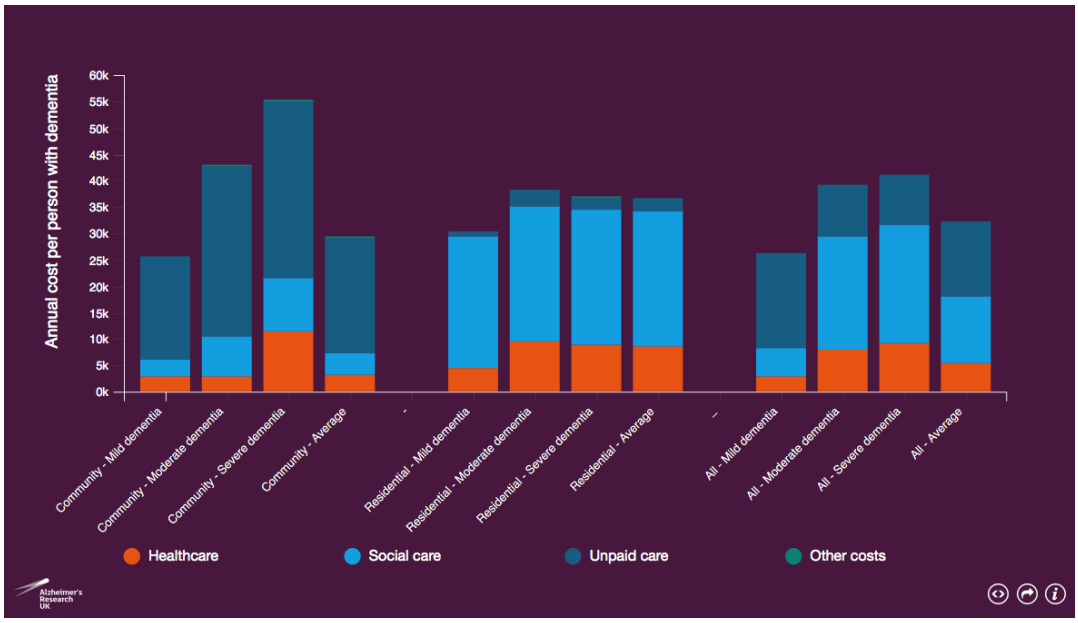


Figure 1: Breakdown of the estimated costs by residence and dementia severity per person, in the UK (30) (Reproduced with Permission)

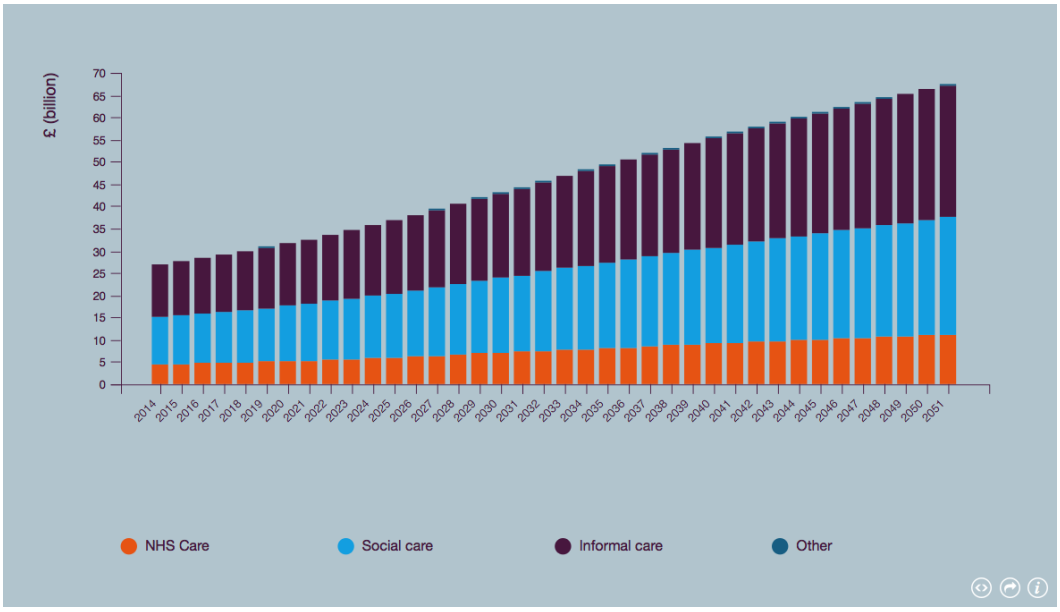


Figure 2: UK cost projections for dementia: the total annual cost for different sectors (30) (Reproduced with Permission)

1.3 Behavioural and Psychological Symptoms of Dementia (BPSD)

1.3.1 What is BPSD?

Behavioural and Psychological Symptoms of Dementia (BPSD) are defined as "*signs and symptoms of disturbed perception, thought content, mood or behaviour*" in people with dementia (31). BPSD includes psychological symptoms such as depression, psychosis, anxiety as well as behaviours such as agitation, aggression, repetitive questioning, wandering and a variety of inappropriate or disinhibited behaviours (32). BPSD is known by other terms such as Neuropsychiatric Symptoms (NPS), challenging behaviours, behaviours that challenge, responsive behaviours,

behavioural symptoms and non-cognitive symptoms (33, 34), however for the purpose of this thesis, the term BPSD shall be used.

1.3.2 How Prevalent is BPSD?

BPSD is highly prevalent in dementia, with the majority of people with dementia experiencing at least one symptom or behaviour throughout their disease progression (35). For example, the Cache County study conducted in the United States (US), found that the 5-year prevalence of BPSD in a cohort of 408 people with dementia was 97% (36). The most commonly observed symptoms in this study were apathy, depression and anxiety (36). In another UK-based study of 231 people with dementia, the prevalence of clinically significant BPSD was found to be 79% (37). In this study, depression was most common in mild dementia, while delusions arose most frequently in moderate dementia and aberrant motor behaviour was the most common in severe dementia (37).

1.3.3 What Causes BPSD?

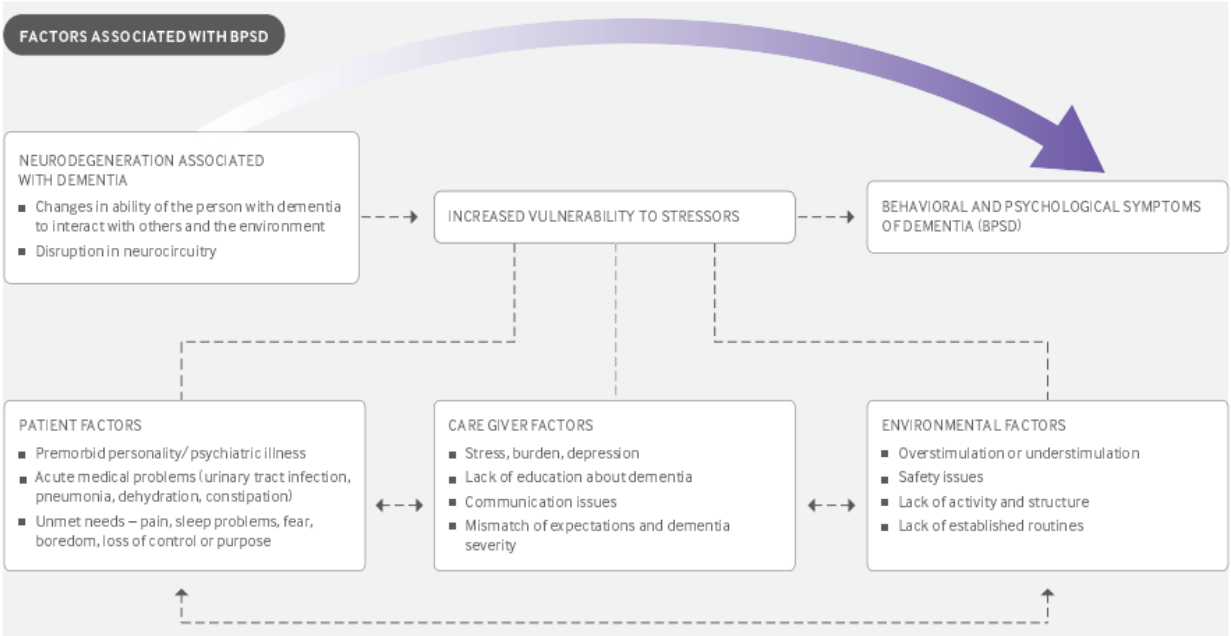


Figure 3: Conceptual model describing how interactions between the person with dementia, care giver, and environmental factors cause BPSD (32) (Reproduced with Permission)

The causes of BPSD are complex and often poorly understood (32). However a recently developed conceptual model by Kales *et al.* in 2015, based on a comprehensive review of the literature and expert opinion, may help us to better understand the factors associated with BPSD, and hence enable more tailored approaches to management (**Figure 3**) (32). The authors of this study argue that neurodegeneration associated with dementia changes a person's ability to interact with others and the environment, and it may also disrupt the brain circuitry involved in emotion and behaviours. Hence the person has an increased vulnerability to stressors (i.e. patient factors, caregiver factors and environmental factors), which all increases the person's risk of developing BPSD. This model describes how these

factors can interact with one another or act independently to cause these symptoms in people with dementia (**Figure 3**).

Some of the patient factors may include premorbid personality or psychiatric illness (e.g. schizophrenia), acute medical problems (e.g. urinary tract infections) or unmet needs (e.g. pain, fear, and boredom). In particular the *'Need-driven Dementia-compromised Behaviour'* (NDB) model has been developed to explain how BPSD can be viewed as an *"expression of unmet needs or goals*" in people with dementia (38). In essence, this model describes how a person with dementia's inability to communicate their needs or goals can manifest as various behaviours and symptoms (e.g. agitation and aggression) (38).

In relation to caregiver (or carer) factors, these are related to the interaction between the carer and the person with dementia, which can often be suboptimal for various reasons (32). Carers of people with dementia experience higher levels of depression and anxiety and generally have poorer levels of wellbeing than non-carers, and this can impact on the quality of the relationship between the carer and the person with dementia (39, 40). Furthermore, a lack of education about dementia, negative communication styles (e.g. shouting) and a mismatch between carer expectations and the severity of dementia illness can all trigger or worsen symptoms in people with dementia (32).

Finally environmental factors may contribute towards the development of BPSD in a person with dementia (32). The *'Progressively Lowered Stress Threshold'* model describes how as the disease progresses and a person with dementia's ability to process environmental stimuli decreases, the stress threshold becomes lower and so

the potential for higher levels of frustration increases (41). Hence over- or under-stimulation, lack of activity and lack of routine can all trigger BPSD in people with dementia (32).

1.3.4 What is the Impact of BPSD?

BPSD can have a profound effect on people with dementia, causing emotional distress in the person and an increased risk of harm to self and/or others (15, 42, 43). The presence of BPSD is also associated with lower quality of life in people with dementia (44). BPSD can also have a significant negative impact on carers (11, 15, 30). Twice as many carers of those with dementia compared with carers of people without dementia experience substantial emotional, physical and financial challenges (45). Approximately one-third of carers of people with dementia suffer from depression compared with 5-17% of non-carers of a similar age (40, 46, 47). Furthermore, carers of people with dementia have lower health-related quality of life than non-carers (48).

A mixed-methods systematic review conducted by Feast *et al.* in 2016 explored the reasons why family carers struggle to deal with BPSD. The authors concluded that the primary reason why family carers were challenged by BPSD was the underlying belief that their loved one had lost, or would inevitably lose, their identity to dementia and thus would become *"dehumanised"* (49). Another systematic review by the same authors found that depressive behaviours in people with dementia were the most distressing for carers, followed by agitation/aggression and apathy (50). Therefore, it is not surprising that high levels of behavioural disturbance in people with dementia,

and in particular carers' emotional reactions to these behaviours, is a strong predictor of institutionalisation (51, 52).

However it is important to acknowledge that paid carers in formal settings such as nursing homes can also be adversely affected by BPSD (53). Nursing home staff in these setting experience high levels of stress and burn-out as a result of dealing with BPSD (54-56). Inadequate education and training to deal with BPSD, along with limited resources have all contributed to high turnover rates among nursing home staff, ultimately compromising the quality of care delivered to residents (11, 57, 58).

1.3.5 How is BPSD treated?

Due to the complex and multifactorial nature of BPSD, the management of BPSD can be quite challenging (32). However there is strong consensus from international guidelines that first line management of BPSD should involve non-pharmacological approaches (e.g. music therapy, reminiscence therapy and carer education/training) (14, 15, 32, 59). There is good evidence to support the use of music therapy for reducing depressive symptoms, behavioural issues and anxiety, as well as carer-based interventions/staff training in communication skills for reducing agitation (60, 61). Only in cases where there is severe distress, aggression, agitation or psychosis or an identifiable risk of harm to the individual with dementia and/or others, should pharmacological approaches be attempted (14, 59), and this will be discussed in detail below. Reversible causes of BPSD (e.g. environmental stressor, urinary tract infection, pain or delirium) should always be ruled out and treated initially (14, 32, 59). A person-centred approach is advocated when caring for people with dementia as each person's needs are very individual, and a *'one size fits all'* solution to BPSD

does not exist (14, 32, 62). In a similar fashion, although there may be stronger evidence to support the use of some non-pharmacological approaches over others (e.g. music therapy versus aromatherapy) (60, 61), there is a need to tailor the approach to meet the unique needs and preferences of the person with dementia (14, 59). Unfortunately these approaches can be resource-intensive and sometimes costly (63). Furthermore, selection of an evidence-based non-pharmacological intervention is made more difficult by the fact that the overall evidence supporting the efficacy of these interventions is somewhat hampered by poor methodological quality and inadequate sample sizes (60). This lack of resources and scepticism regarding the efficacy surrounding non-pharmacological approaches has been found to be a significant barrier to utilising these approaches in practice (64).

1.4 Potentially Inappropriate Prescribing (PIP) in Dementia

1.4.1 What is PIP and how Common is it in People with Dementia?

Medications are considered to be appropriately prescribed when they have a clear evidence-based indication, are cost effective and are well tolerated (65). Potentially inappropriate prescribing (PIP) is defined as *"the practice of administering medications in a manner that poses more risk than benefit, particularly where safer alternatives exist" (66).* A large number of implicit (judgement-based) and explicit (criterion-based) tools been developed and validated to measure PIP in older adults e.g. Beers (67) and Screening Tool of Older People's Prescriptions (STOPP) / Screening

Tool to Alert to Right Treatment (START) criteria (68). Although these tools have been developed for the general older population, they do include some criteria specifically for people with dementia e.g. psychotropics and anticholinergics (67, 68). Coupled with age-related changes in pharmacokinetics and pharmacodynamics, people with dementia are particularly susceptible to the cognitive and cardiac adverse effects of these medications (69, 70).

Although there is limited literature examining the prevalence and consequences of PIP specifically in people with dementia, recent studies have shown that PIP is highly prevalent in this population and is associated with adverse health outcomes, especially hospitalisations (69-73). Furthermore, despite the plethora of PIP tools available for the general older population, there are only a few tools specific to people with dementia, and most of these focus on the advanced stages of dementia (74, 75).

In terms of PIP in dementia, of particular concern is the inappropriate prescribing of psychotropic medications (i.e. antipsychotics, antidepressants, hypnotics, anxiolytics and anti-convulsants/mood-stabilisers). There have recently been tools developed specifically to measure the appropriateness of psychotropic prescribing in people with dementia (76, 77). An implicit tool called the Appropriate Psychotropic drug use in Dementia (APID) index, was developed to address the realisation that the high frequency of psychotropic utilisation in people with dementia, does not necessarily imply that it is inappropriate (76). In a cross-sectional study of 559 nursing home residents with dementia across the Netherlands, only 10% of psychotropic drug use for BPSD was found to be fully appropriate according to the APID index (78). Of the

seven domains of appropriateness measured in the APID index, it was found that *indication*, *evaluation* and *therapy duration* contributed most to PIP (78). Upon further analysis, the authors determined that older age and more pronounced BPSD were associated with more appropriate psychotropic prescriptions, however the authors concluded that more research was required to determine the influence of patient and healthcare professional factors on appropriate prescribing (79). An explicit tool known as the Quality Use of Medications in Dementia (QUM-D) has also been developed and focuses on ten factors specifically relating to the quality of psychotropic prescribing in people with dementia (77). When tested on a subgroup of people with dementia, this tool showed high inter-rater reliability (intra-class correlation coefficient = 1.0) and was also found to improve the appropriateness of prescribing from baseline to follow up (77).

1.4.2 Antipsychotic Prescribing in People with Dementia

Of all psychotropic medications, antipsychotics in particular are commonly prescribed for the management of BPSD (80-82). As discussed above, antipsychotics are considered to be second line for the management of BPSD, except in cases of severe distress, aggression, agitation or psychosis or when there is an identifiable risk of harm to the person with dementia and/or others (14, 59, 83).

However the prescribing of antipsychotics to people with dementia remains a controversial topic with some arguing the case for judicious prescribing (84), citing significant flaws in the evidence-base (85), and the important role they play in treatment (86) as justification for their continued usage. Whereas others contest that these agents should rarely be used (87), some even argue that their use may

constitute a human rights infringement (88) and others have called for much tighter regulatory restrictions (89). A multitude of qualitative studies have been conducted to explore these wide range of views (64, 90, 91), however a better understanding of decision-making in this complex healthcare area is clearly required.

1.4.3 *'Off-label'* Prescribing

The vast majority of antipsychotic prescribing in people with dementia is *'off-label'* (92) – meaning that the medication is prescribed in a manner different from that approved by national regulatory bodies e.g. Food and Drug Administration (FDA) in the US (93). *'Off-label'* prescribing is legal and common practice, particularly for rare conditions (e.g. amyotrophic lateral sclerosis) or for populations that may lack clinical trials (e.g. paediatrics and older people) (93). However there are ethical and legal difficulties surrounding *'off-label'* prescribing, mainly the fact that the prescriber (as opposed to the manufacturer) is liable should harm occur (94). Furthermore when prescribing *'off-label'*, prescribers should always seek informed consent from patients, which may not always be feasible (94).

The only antipsychotic that is currently licensed for BPSD in Ireland is risperidone (95). Furthermore the license stipulates that risperidone is only *"indicated for the short-term treatment (up to six weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others"* (95). In the US however, there are currently no antipsychotics licensed for the management of BPSD, and instead they all carry a *'black-box'* warning regarding the risk of harm when used in people with dementia (96).

1.4.4 Prevalence of Antipsychotic Prescribing in People with Dementia

There have been a plethora of cross-sectional studies conducted across various settings and countries, all showing the prevalent prescribing of antipsychotics in people with dementia. A systematic review and meta-analysis conducted by Kirkham *et al.* in 2017 found antipsychotic prescribing to be widespread across many countries, and calculated the pooled estimates of antipsychotic prescribing to be significantly lower in community settings compared to nursing home settings (12.3% versus 37.5%; $Q = 61.77$, $p < 0.0001$) (**Figure 4**) (97). There was also great variability between studies, with the prevalence of antipsychotic prescribing ranging from 3.74% to 32.47% in community settings and from 23.64% to 64.0% in nursing home settings. The authors of this review found that increasing dementia severity was associated with higher levels of antipsychotic prescribing.

Author	Number Receiving AP	Total Sample Size	Prevalence (%)	95% CI	Weight
Setting = Community					
Semla 1995	43	325	13.23	[10.02; 17.48]	2.4%
Forsell 1997	14	154	9.09	[5.52; 14.98]	1.3%
Hartikainen 2003	25	77	32.47	[23.53; 44.81]	2.1%
Linden 2004	12	140	8.57	[4.99; 14.72]	1.2%
Schubert 2006	4	107	3.74	[1.43; 9.78]	0.5%
Chan 2007	14	285	4.91	[2.95; 8.19]	1.3%
Dhawan 2008	29	173	16.76	[12.03; 23.36]	2.1%
Arbus 2010	46	686	6.71	[5.07; 8.86]	2.4%
Rhee 2011	58	307	18.89	[14.98; 23.82]	2.7%
Martinez 2013	6293	50349	12.50	[12.21; 12.79]	3.8%
Maxwell 2013	23580	104802	22.50	[22.25; 22.75]	3.8%
Random effects model		**157405**	**12.31**	**[9.36; 16.19]**	**23.6%**
Heterogeneity: I-squared=99.5%, tau-squared=0.1764, Q=2148.21, df=10, p<0.0001					
Setting = Long-Term Care					
Arling 1991	472	1997	23.64	[21.84; 25.57]	3.7%
Ballard 2001	52	209	24.88	[19.66; 31.49]	2.7%
Margolla-Lanna 2001	87	209	41.63	[35.45; 48.88]	3.2%
Hosia-Randell 2005	598	1380	43.33	[40.80; 46.03]	3.7%
Alanen 2006	255	782	32.61	[29.48; 36.07]	3.5%
Kim 2006	40	107	37.38	[29.25; 47.77]	2.6%
Alldred 2007	46	146	31.51	[24.80; 40.02]	2.7%
Selbaek 2007	240	933	25.72	[23.07; 28.69]	3.5%
Kamble 2009	227722	692566	32.88	[32.77; 32.99]	3.8%
Nijk 2009	826	1322	62.48	[59.92; 65.15]	3.8%
Nobili 2009	209	349	59.89	[54.96; 65.25]	3.6%
Seitz 2009	230830	665217	34.70	[34.59; 34.81]	3.8%
Ballale 2010	32	50	64.00	[51.99; 78.79]	2.9%
Bell 2010	334	781	42.77	[39.43; 46.38]	3.6%
Chen 2010	3313	7659	43.26	[42.16; 44.38]	3.8%
Majic 2010	159	304	52.30	[46.98; 58.23]	3.5%
Azermai 2011a	383	825	46.42	[43.14; 49.96]	3.7%
Azermai 2011b	570	1730	32.95	[30.81; 35.24]	3.7%
Barro-Belaygues 2011	269	1005	26.77	[24.16; 29.65]	3.5%
Zuidema 2011	476	1322	36.01	[33.51; 38.69]	3.7%
Bourgeois 2012b	569	1730	32.89	[30.75; 35.18]	3.7%
Gustafsson 2013	514	2019	25.46	[23.63; 27.43]	3.7%
Random effects model		**1382642**	**37.35**	**[35.93; 38.84]**	**76.4%**
Heterogeneity: I-squared=99.1%, tau-squared=0.0062, Q=2310.11, df=21, p<0.0001					
Subgroup Differences: Q=61.77, df=1, p<0.0001					

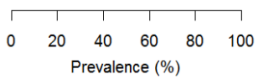


Figure 4: Forest plot of the prevalence of antipsychotic prescribing in community and long-term care (nursing home) settings (97) (Reproduced with Permission)

Another systematic review by Janus *et al.* in 2016 examined the prevalence of antipsychotic prescribing in nursing homes across Western Europe (80). The authors calculated the pooled estimate of antipsychotic prescribing to be 27% (95% Confidence Interval [CI] = 27-28) across all 38 studies. The highest rate of antipsychotic prescribing was found in Austrian studies (pooled estimate = 45%) and the lowest rates were found in French and Norwegian studies (pooled estimates = 25% for both). Once again, there was substantial variation between studies with the prevalence ranging from 11.9% to 54.0%. The pooled average of 27% is lower than

that calculated by Kirkham *et al.* (37.35%), but this may be explained by the fact that Janus *et al.* also included studies of nursing home residents without distinction as to their level of cognitive impairment, whereas Kirkham *et al.* only included residents with a confirmed diagnosis of dementia (97). As nursing home residents without dementia tend to be prescribed less antipsychotics than residents with dementia, this may explain the lower pooled average reported by Janus *et al* (98).

By comparison, there is limited published data on the prevalence of antipsychotic prescribing in Irish nursing home or community settings. A retrospective study conducted by our research group found that of 375 residents with dementia residing in 14 publicly funded nursing homes across Cork, 159 (42.4%) were prescribed an antipsychotic (99). However it is important to note that this study had several limitations. Firstly the researchers were reliant on a documented diagnosis of dementia in the medical notes, however these diagnoses are commonly under reported (100). Furthermore, the data were collected in 2009/2010 in 14 publicly funded nursing homes in one county in Ireland, hence there is uncertainty regarding the generalisability of these findings today across all 577 nursing homes in Ireland (101).

Furthermore, there have been relatively few cross-sectional studies conducted in acute care settings globally. White *et al.* report that in a cohort of 230 people with dementia admitted to two acute hospitals in the UK, 12.2% of these patients were prescribed an antipsychotic at any time during admission (102). In another UK based study, which retrospectively analysed prescribing to people with dementia in 34 acute English hospitals, 16.6% of inpatients with dementia were found to be

prescribed an antipsychotic during their admission (103). The Irish National Audit of Dementia Care (INAD) study conducted in all 35 public acute hospitals across Ireland in 2013, determined that 41% of inpatients with dementia were prescribed antipsychotics (104, 105). It is important to note however, that the population selected for this audit may not have been representative of all hospitalised dementia patients due to the specific audit requirements (i.e. explicit dementia diagnosis and a minimum length of stay of five days).

1.4.5 Evidence of the Harms and Benefits of Antipsychotic Usage in Dementia

Concerns about the use of antipsychotics in people with dementia began in the early 2000s when the European Medicines Agency (EMA) and the US FDA issued drug safety warnings about atypical (newer generation) antipsychotics in 2004/2005 (106), which expanded to include all antipsychotics in 2008/2009 (107, 108). Substantial evidence points to an increased risk of harm and limited benefit as a result of antipsychotic usage for the management of BPSD (109-112). In a review of 16 meta-analyses that evaluated the use of antipsychotics in people with dementia, Tampi *et al.* found that antipsychotics demonstrated only modest efficacy in treating BPSD (113). The use of these agents in people with dementia is often limited by their adverse effect profile, particularly the increased risk of stroke (3-fold increase) and death (2-fold increase) compared to placebo (112-115). Other adverse effects of antipsychotics include sedation, pneumonia, hip fractures, abnormal gait and extrapyramidal side effects (e.g. movement disorders) (113, 116, 117).

Of all psychotropics used for the management of dementia, atypical antipsychotics have the strongest evidence of efficacy, albeit the benefits are modest (standardised effect size 0.13 to 0.16) (118). The best available evidence from clinical trials would suggest that risperidone is the most effective - and quetiapine the least effective - antipsychotic for treating BPSD, especially aggression or psychosis (15, 113, 119). Even when treatment with antipsychotics is effective, guidelines strongly advocate that treatment is tapered and withdrawn after a period of about 12 weeks (14, 59), as the evidence suggests that these drugs can be safely withdrawn in most people without the return of BPSD (120). However the evidence does point to an increased risk of behaviour recurrence in those with severe BPSD at baseline, or in those who have responded well to long-term antipsychotic use (120).

To illustrate the risk-benefit ratio of antipsychotic usage in dementia, the Centre for Effective Practice in Canada have developed an info-graphic (**Figure 5**) (121). Essentially the evidence suggests that for every 100 people with dementia treated with an antipsychotic for BPSD, 20 will gain benefit, and 80 will gain no benefit - one of whom is likely to die or have a stroke. The risk of death appears to be drug- and dose-dependent with haloperidol conferring the greatest risk. Compared with non-users, people with dementia receiving haloperidol were found to have an increased mortality risk of 3.8% (95% CI [confidence intervals] = 1.0% - 6.6%) with a number needed to harm (NNH) of 26 (95% CI = 15 - 99). Of all antipsychotics, quetiapine conferred the lowest risk of mortality of 2.0% (95% CI = 0.7%-3.3%) with an NNH of 50 (95% CI = 30-150) (109). Furthermore, the use of haloperidol as the first choice antipsychotic in dementia is not recommended due to the significantly higher risks

of extrapyramidal side effects caused by this drug, compared to atypical antipsychotics (14, 59).

Figure 5: The Risk-Benefit Ratio for Antipsychotic Usage in Dementia (121) (Reproduced with Permission)

1.4.6 Evidence of the Harms and Benefits of the use of Other Psychotropic Medicines in Dementia

There is very limited evidence of efficacy to support the use of any other psychotropic agent (antidepressants, anti-dementia drugs, anticonvulsants, hypnotics and anxiolytics) for the management of BPSD; furthermore they all cause various side effects, particularly sedation (14, 15, 59). However, the CitAD trial found that citalopram at a dose of 30mg daily significantly reduced agitation in people with dementia compared to placebo (122). Yet at this high dose of citalopram (20mg is the

maximum dose licensed for older adults), cognitive and cardiac adverse effects were significantly more common in the treatment group, and hence this may limit its usage in practice. Trials are currently being conducted with other psychotropics such as carbamazepine and mirtazapine (NCT03031184), however until there is sufficient evidence of efficacy and safety to support the use of any of these drugs for these indications, they should be avoided (unless for co-morbid conditions e.g. depression or epilepsy) (15).

1.5 The Evolving Dementia Policy Landscape

1.5.1 Policy Approaches in Different Countries

There has been an evolving policy approach to dealing with the issue of inappropriate antipsychotic prescribing for people with dementia, with a particular emphasis on nursing home settings (123). Across different countries, there have been various approaches adopted, some being more successful than others (123)

In the US, the Omnibus Reconciliation Act (OBRA) of 1987 was introduced to regulate antipsychotic prescribing in nursing home residents. In essence, prescribing an antipsychotic in a nursing home required a specific diagnosis and behavioural indication as a result of OBRA (124). The FDA issued a '*black-box*' warning about atypical antipsychotics in 2005 (106), which expanded to include all antipsychotics in 2008 (107). More recently in 2012, the Centres for Medicare and Medicaid Services (CMS) launched a national partnership programme to improve the quality of care for nursing home residents with dementia (125). This programme entailed

comprehensive training for nursing home staff, public reporting of antipsychotic use and a '*five-star*' quality rating system for nursing homes (126).

Drug safety warnings regarding the use of antipsychotics in dementia were also released across the UK (and all European Union [EU] countries) in 2004 and 2009, similar to the FDA warnings (108, 127). Subsequently, the seminal Banerjee report released in 2009, discussed the limited evidence base to support the widespread usage of antipsychotics and estimated that 180,000 people with dementia in the UK were prescribed an antipsychotic annually, with 1,800 of those dying every year as a consequence of taking this medication (128). This report called for urgent action and suggested a goal of reducing antipsychotic prescribing levels by two thirds within three years (128). Various dementia strategies and other policy documents in the UK have re-emphasised the importance of reducing these levels, with governance changes, as well as audit and feedback loops being implemented to encourage ongoing monitoring of antipsychotic prescribing (129-132).

In Ireland, the National Dementia Strategy was launched in 2014 with the overarching aim of "*improving dementia care so that people with dementia can live well for as long as possible, can ultimately die with comfort and dignity, and can have services and supports delivered in the best way possible*" (133). The strategy explicitly pointed to the risks associated with the use of antipsychotics in people with dementia, and a priority action plan of the strategy was to develop guidance material on the appropriate use of psychotropic medication in people with dementia. These national clinical guidelines are planned to be published towards the end of 2018 or early 2019.

1.5.2 Health Information and Quality Authority (HIQA)

HIQA established in 2007, is the independent national regulator of health and social care including nursing homes, in Ireland. The aim of HIQA is to drive continuous improvement in Ireland's health and social care services. HIQA's role includes developing standards and guidance, as well as inspecting and reviewing health and social care services (134).

Of particular relevance to the prescribing of antipsychotics to people with dementia is the HIQA Guidance on Restraint Procedures (135). In this document, chemical restraint is defined as "*the use of medication to control or modify a person's behaviour when no medically identified conditions is being treated, or where the treatment is not necessary for the condition or the intended effect of the drug is to sedate the person for convenience or disciplinary purposes" (135).* Giving a resident who wanders a sedative is outlined as an example of chemical restraint. Further guidance is specified in HIQA's National Standards for Residential Care Settings for Older People in Ireland, with a particular importance placed on promoting bodily integrity, personal liberty and a restraint-free environment (136).

Reporting of chemical restraint incidents in nursing homes have recently become mandatory in Ireland. The regulations governing the reporting of restraint incidents are contained in the Health Act 2007 (Care and Welfare of Residents in Designated Centres for Older People) Regulations 2013 (137).

- Regulation 7 (3) states: The registered provider shall ensure that, where restraint is used in a designated centre, it is only used in accordance with

national policy as published on the website of the Department of Health from time to time.

- Schedule 3.4 (g) of the regulations requires that the nursing home keep *"a record of any occasion on which restraint is used, the resident to whom it is applied, the reason for its use, the interventions tried to manage the behaviour, the nature of the restraint and its duration".*
- Schedule 4.2 (k) requires that the nursing home shall notify the Chief Inspector (in HIQA) on a quarterly basis of *"any occasion when restraint was used"*.

In this way, the nursing home's registered provider is obliged by law keep a record of any form of restraint and report this to the Chief Inspector on a quarterly basis.

1.5.3 The Impact of National Approaches on Antipsychotic Prescribing

Various drug safety warnings (106, 107), national policy programmes (128) and regulatory initiatives (125) have been put into effect across many countries, in an attempt to curb the excessive usage of antipsychotics. Significant reductions over time have been observed in Canada (97, 138), the US (126, 139, 140), France (141) and the UK (108, 127, 142-144). However not all studies have consistently shown reductions in antipsychotic prescribing, with some conducted in Germany (145), Norway (146) and the UK (147) showing no significant changes, while others conducted in Italy (127), France (148) and Japan (149) have actually shown an increase in prescribing over time. Conflicting results within countries may be due to different populations of interest (e.g. community-dwelling versus residential) or different methods of data collection (142, 147). Nonetheless, concerns have been

raised regarding the substitution of antipsychotics with other less evidence-based psychotropics such as anticonvulsants or antidepressants (126, 142), and also the increased level of schizophrenia diagnoses in US nursing home settings observed in recent times, possibly to avoid mandatory reporting of antipsychotic usage (150). Although there seems to be an overall reduction in antipsychotic usage for the main part, it is still unclear how such programmes, regulations and policies impact on individual healthcare professionals' decision-making process. Moreover there is a lack of research conducted on the negative unintended consequences of such national approaches. Similarly in Ireland while there has been a move towards greater regulation of antipsychotic prescribing in nursing homes in line with other jurisdictions, the impact of these changes is yet to be evaluated.

1.6 Interventions to Improve the Appropriateness of Prescribing in People with Dementia

1.6.1 Nursing Home Setting

Interventions aimed at improving the appropriateness of prescribing in people with dementia have predominantly focused on antipsychotics (or psychotropics more broadly), and have been conducted primarily in the nursing home setting (151, 152). A systematic review published in 2014 by Thompson-Coon *et al.* found 22 studies evaluating the effectiveness of interventions to reduce inappropriate prescribing of antipsychotics to nursing home residents with dementia (151). These interventions were categorised as educational programmes (n = 11), in-reach services (involving interdisciplinary teams providing outreach services to nursing homes) (n= 2),

medication reviews (n = 4) and multicomponent interventions (n = 5) (151). Irrespective of the nature of the intervention, the majority were found to result in relative reductions in antipsychotic prescribing levels of between 12% and 20%. However, the authors added that there was "*little information in the included studies to aid understanding of the sustainability of the effects of interventions,*" and recommended further qualitative work be conducted to explore the barriers and facilitators to appropriate antipsychotic prescribing, as well as a more in-depth exploration of nursing home culture (151). Additionally the authors remarked on the lack of detail provided for many of the interventions, preventing future replication by other researchers. Similar to the findings of a Cochrane review on the more general topic of interventions to optimise prescribing in nursing homes (153), the authors of the systematic review were unable to make definitive recommendations for practice due to the diversity of interventions and the often poor quality of included studies (151). However both reviews commented on the potential benefits of interdisciplinary interventions, particularly those involving pharmacists (151, 153).

A more recent systematic review examined the effects of psychosocial interventions on psychotropic prescribing for nursing home residents with dementia (152). The authors found that compared to usual care, the interventions that focused on changing the culture of nursing homes were more effective at reducing antipsychotic prescribing (relative risk [RR] = 0.71; 95% CI = 0.57 – 0.73), than those which simply provided education and training (RR = 1.50; 95% CI = 0.49 – 4.64) (152). The authors explained this finding by stating that dementia education on its own is of limited benefit because of its short-term effects (154). Furthermore the authors found that involving the prescribers in such interventions resulted in a significantly greater

reduction in antipsychotic prescribing (RR = 0.66; 95% CI = 0.54 – 0.80). The authors concluded that involving the prescriber in these psychosocial interventions is potentially key to changing prescribing behaviour within the context of a nursing home.

1.6.2 Acute and Community Settings

Meanwhile interventions to improve the appropriateness of prescribing in people with dementia in either acute or community settings are relatively limited. Considering that almost two-thirds of all people with dementia live in the community (28), and a quarter of all hospitalised older adults have dementia (100), the limited number of interventions in these settings is surprising. A systematic review of interventions to manage BPSD in community-dwelling adults with dementia was recently published by Trivedi *et al.* (155). Of 48 randomised controlled trials (RCTs) included in this systematic review, only one discussed medication usage in people with dementia as an outcome, specifically antipsychotics, and this study is discussed below (156). Furthermore, to the best of our knowledge, the few interventions conducted in acute settings have not yet been collated into a systematic review.

One RCT conducted in the US, randomised 153 community-dwelling adults with dementia to the intervention (interdisciplinary collaborative care management focused on guideline recommendations, led by an advanced nurse practitioner) or usual care (156). Intervention patients experienced significant fewer behavioural symptoms and a reduction in carer stress compared with patients who received usual care after 12 months of this programme. However there was no significant differences in the utilisation of antipsychotics between groups (156). A non-

randomised evaluation conducted within primary care in the UK (which was not included in the systematic review), evaluated the effect of a pharmacy-led program to review low-dose antipsychotics in people with dementia (157). From a total of 1,051 people with dementia screened, 70 were receiving low-dose antipsychotics which were initiated by primary care, and in 43 people (61% of 70) their antipsychotics were withdrawn or dose reduced (157). However this was a one-armed study with no follow up, therefore caution is advised when interpreting these results. Additionally, this study was not exclusively for community-dwelling people with dementia as it also included people with dementia residing in nursing homes.

A before-after study conducted in Switzerland, examined the effect of collaborative interdisciplinary geriatric and psychiatric care on PIP in 150 consecutively hospitalised older adults with dementia (158). The intervention was found to significantly reduce the incidence of PIP according to the STOPP/START criteria ($p < 0.0001$). Of note, the prevalence of patients prescribed at least one long-term (>1 month) antipsychotic reduced from 14.7% to 1.4% ($p < 0.0001$) (158). However, there were several limitation with this study such as the uncontrolled nature of this intervention and the non-random selection of participants. These limitations should be considered when interpreting these findings.

1.7 Summary and Gaps in Knowledge

In summary, dementia is highly prevalent and is projected to increase dramatically over the next few decades. BPSD affects almost all people with dementia at some stage throughout their disease progression, and these behavioural symptoms can have a significantly negative impact on the person with dementia and others. The

causes of BPSD are complex and often poorly understood, and its management is frequently suboptimal. Antipsychotics in particular, continue to be frequently prescribed inappropriately to people with dementia for the management of BPSD, especially in nursing home settings. This is in spite of substantial evidence of the harms caused by antipsychotics, and various national approaches to curb excessive usage. The reasons for the persistent inappropriate prescribing of these medicines are still unclear. Furthermore, despite the large number of interventions conducted in this setting, there are still some uncertainties regarding the precise components of an intervention required in order to successfully change behaviour, the impact context has on implementation of the intervention, as well as the sustainability of effects.

Hence, there is a need for a theoretically-informed, evidence-based intervention to sustainably rationalise (or improve the appropriateness of) antipsychotic prescribing in people with dementia. In order to successfully achieve this aim, there are several important gaps in our knowledge which firstly need to be addressed.

- We need to learn about the effectiveness of pharmacists' interventions in improving the quality of prescribing in people with dementia, as this may prove to be an effective approach to undertake going forward. We know that pharmacists' interventions are effective in nursing home settings (151, 153), however the evidence surrounding their effectiveness in acute settings is unclear.
- We also need to better understand the Irish context by examining psychotropic prescribing patterns in people with dementia. We have some

Irish data to show that antipsychotic and psychotropic prescribing is highly prevalent in nursing home settings (99), however there are limited Irish data in other settings.

- We need to determine what setting would be the best in which to develop and undertake an intervention to rationalise antipsychotic prescribing in people with dementia. Although Chapter 2 focuses on the acute setting and Chapter 3 focuses on a hospitalised population that is predominantly community-dwelling based, we will be mindful of the fact that the burden of antipsychotic prescribing occurs in the nursing home setting (97). The remainder of the thesis will then focus on the chosen sector in order to remain focused.
- We need to draw on existing international qualitative evidence to understand why antipsychotics continue to be inappropriately prescribed to people with dementia. Understanding this behaviour will be an important step in the development of our intervention.
- We need to explore Irish-specific barriers and facilitators to appropriate antipsychotic prescribing in people with dementia. Having collated the international perspective, it will be important to understand the local prescribing context and to explore recent phenomena which may impact on prescribers' decision-making.
- We need to determine what an evidence-based and theory-informed intervention to rationalise antipsychotic prescribing in people with dementia looks like. Drawing on our previous work, international literature (151, 159) and theory (160-162) we need to establish the optimal composition of this

intervention, and define a potential mechanism of behaviour change. In particular we need to be careful in deciding who will be delivering the intervention and the way in which it is delivered. Although the temptation may be to conduct a pharmacist-led medication review, due to our focus on these types of interventions in Chapter 2, there may be important cultural factors arising from our qualitative work in Chapter 5, potentially affecting acceptability and/or feasibility, which may change our thinking on this matter.

- Finally, we need to assess whether this novel intervention is feasible to conduct and is acceptable to stakeholders within an Irish setting, so that the intervention may be up-scaled and potentially sustainably implemented.

1.8 Methodological Approach

1.8.1 Thesis Aim and Objectives

In light of the gaps in knowledge described above, the overarching aim of this thesis was as follows:

- To develop and assess the feasibility of a theoretically-informed, evidence-based and sustainable intervention to rationalise antipsychotic prescribing in nursing home residents with dementia.

To achieve this overarching aim, the objectives of this thesis were:

1. To systematically review and synthesise the quantitative evidence surrounding the effectiveness of pharmacists' interventions to improve the appropriateness of prescribing in hospitalised older patients, with a particular focus on patients with dementia.

2. To examine prescribing patterns in older patients with and without dementia on admission to hospital, within the Cork Region, with a particular focus on psychotropic drug use and polypharmacy.

3. To systematically review and synthesise the qualitative evidence surrounding the influences on decision-making regarding antipsychotic prescribing in nursing home residents with dementia.

4. To explore the barriers and facilitators to appropriate antipsychotic prescribing in nursing home residents with dementia.

5. To develop a theoretically-informed, evidence-based intervention to sustainably improve the appropriateness of antipsychotic prescribing to nursing home residents with dementia.

6. To assess the acceptability and feasibility of the novel intervention in an Irish nursing home setting.

1.8.2 Methodological Framework

The Medical Research Council (MRC) framework for developing and evaluating complex interventions was used as the overarching framework for my thesis (**Figure 6**) (163). This framework provided guidance on the '*development*' and '*feasibility/piloting*' phases, in order to meet the aim and objectives of this thesis. In particular, it helped with making appropriate methodological and practical choices throughout the thesis, and contributed towards making the findings more generalisable. Importantly, this framework emphasises that these phases are not necessarily linear and are often iterative.

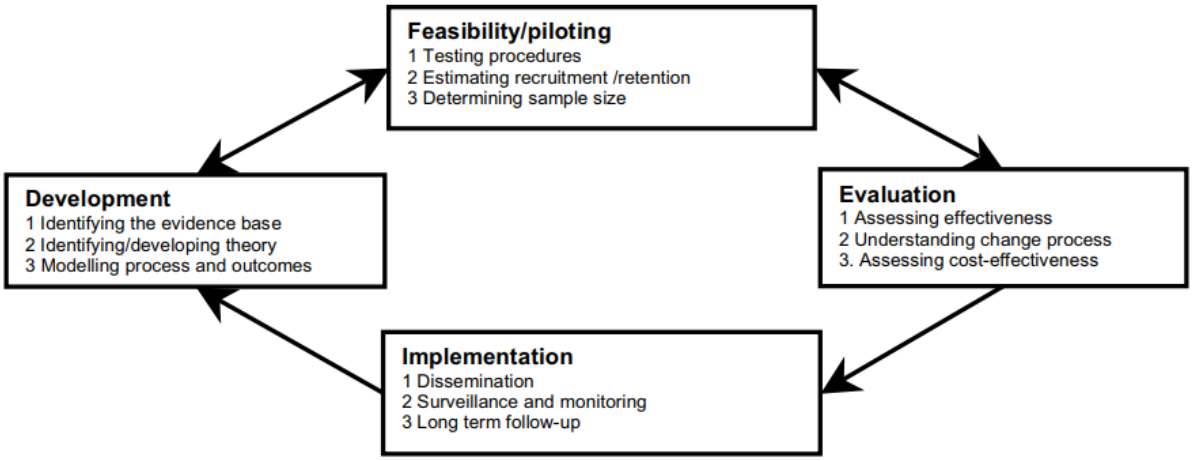


Figure 6: The Medical Research Council (MRC) framework for developing and evaluating complex intervention (163) (Reproduced with Permission)

To help design the intervention, I used the Behaviour Change Wheel (BCW) approach (164) and also incorporated Patient and Public Involvement (PPI) (165). The BCW is an approach to designing behaviour change interventions based on theory and evidence (**Figure 7**). Essentially the BCW provides the intervention designer with theory-informed tools and techniques to help understand and change behaviour in a step-by-step and transparent manner (164).

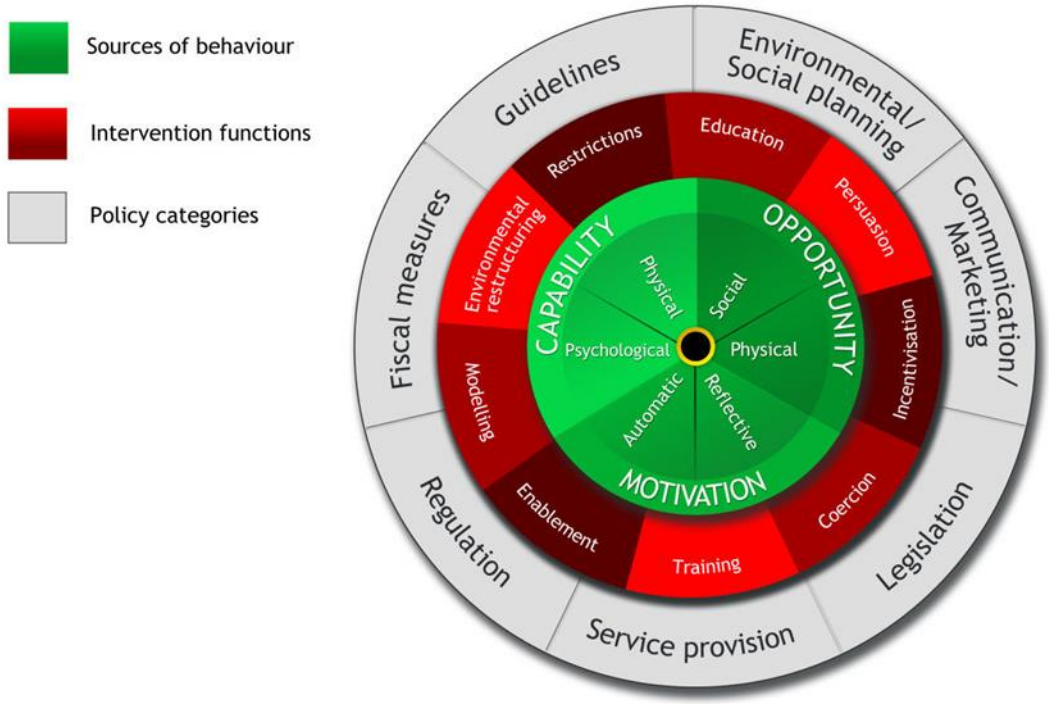


Figure 7: The Behaviour Change Wheel (150) (Reproduced with Permission)

PPI is defined as research that is carried out *'with'* or *'by'* members of the public rather than *'to', 'about'*, or *'for'* them (165). The goal of PPI is to achieve a partnership between the patients/public and researchers, resulting in improved research relevance, quality and outcomes (166). Involving people with dementia in research

in a meaningful way is feasible despite challenges such as verbal communication impairment, memory loss and diminished decision-making capacity (167, 168). Furthermore, involving people with dementia in research through PPI is strongly advocated by Alzheimer Europe and other groups who work to promote the rights, dignity and autonomy of people with dementia (169). In terms of this PhD, I incorporated PPI into the primary qualitative research study (Chapter 5) and intervention design process (Chapter 6). Advisory group members were consulted on a range of topics including the issue of antipsychotic prescribing in people with dementia itself, semi-structured interview topic guides and recruitment, intervention selection and dissemination activities. Members were not reimbursed, however a voucher was provided to all members at the end of their involvement as a small token of appreciation. The strengths and limitations of the PPI component in my research is discussed in Chapter 8.

As discussed, a core component of the thesis was to incorporate evidence and theory into the intervention design. The existing evidence base was identified through evaluating previously conducted high quality systematic reviews such as the one conducted by Thompson-Coon *et al*. (151). If there was a need for a more up-to-date synthesis in order to help answer research questions pertinent to the overarching aim of my thesis, this was also conducted. Identifying and developing theory is recommended by the MRC guidance when developing and evaluating complex interventions in order to *"develop a theoretical understanding of the likely process of change"* (163). The explicit use of theory in intervention development has been argued as a means of reducing the time needed to develop complex interventions, optimise their design, identify the necessary successful contextual conditions and

enhance understanding and generalisability (170, 171). For this thesis, I primarily used the BCW to inform the choice of theoretical approach, however a paper by Per Nilsen also provided a helpful overview of implementation theories, models and frameworks to consider (172). An in-depth description of how I used the BCW and PPI within the overarching MRC framework, for the development of the complex intervention, is provided in Chapter 6.

1.8.3 Research Paradigm

I approached this research from a *pragmatism* paradigm, meaning that the most suitable methods to answer the research questions were employed (173). The two opposing traditional paradigms are that of *positivism* (the notion of a singular reality, requiring an objective and value-free inquiry i.e. quantitative research methods), and *constructivism* (the concept that there is no such thing as a single objective reality, and these multiple realities can only truly be explored through subjective inquiry i.e. qualitative research methods) (174, 175). *Pragmatism* offers an alternative to the debate between *positivism* and *constructivism* and focuses on the problem to be researched, and the utility of the findings, rather than arguing which worldview is more important (175). Pragmatism values both quantitative and qualitative methods as a means of conducting practical, relevant and high quality research (174, 175), and hence a mixed-methods investigation was undertaken for this thesis. In essence, pragmatism as a research paradigm appealed to me as a pharmacist, because of its focus on practicality rather than its broader philosophical basis (173). Taking this approach allowed me to make use of the most appropriate methods for my research, which ended up being mixed-methods. To maintain reflexivity throughout my PhD, I

kept a reflective diary to document my thoughts and decision-making. Reflexivity in mixed-methods research has been found to be an effective, ongoing means of critically reviewing work, processes and researcher development (176).

1.8.4 Study Design

As depicted in **Figure 8**, a sequential explanatory (quantitative followed by qualitative) mixed-methods design was employed for Chapters 2-6, followed by concurrent triangulation (simultaneous qualitative and quantitative) for Chapter 7 (174). The purpose of combining methods for this thesis were twofold; firstly for development (one method used to inform the development of another) and secondly for complementarity (qualitative and quantitative methods used to address different aspects of the same research question) (177). Throughout my thesis, equal weighting was given to both quantitative and qualitative methods (177).

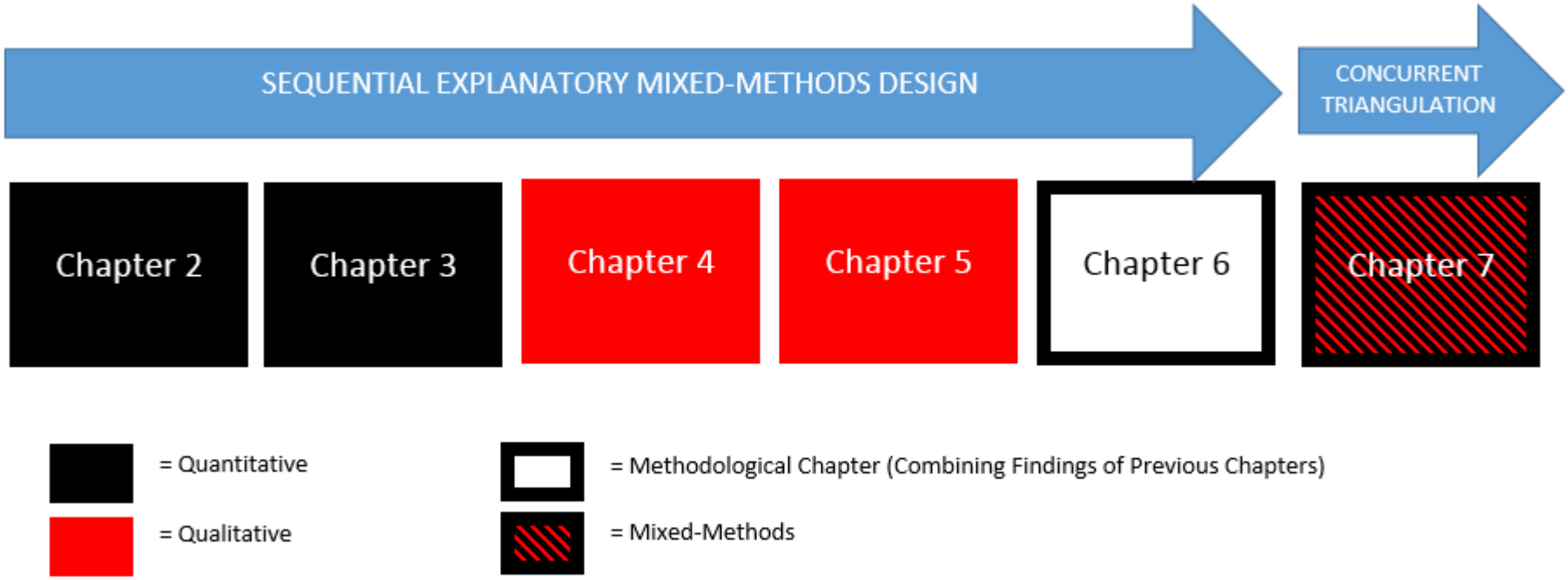


Figure 8: Mixed-Methods Design of Thesis

1.8.5 Thesis Outline

Each of the six objectives outlined above, are aligned to a specific study chapter (Chapters 2 - 7), and each of these chapters is either published in a peer-reviewed journal or drafted for submission (**Figure 9**). The six study chapters are then followed by an overall discussion chapter (Chapter 8). The methods used in this thesis, and the resultant findings are discussed separately in each of the six study chapters. In brief, the outline for the remainder of this thesis is as follows:

Chapter 2: A systematic review and meta-analysis of the effectiveness of pharmacists' interventions in improving the appropriateness of prescribing in older hospitalised patients, with a particular focus on patients with dementia.

Chapter 3: A retrospective cross-sectional analysis of medication data collected for older patients with and without dementia, on admission to six acute hospitals across Cork city and county.

Chapter 4: A systematic review and synthesis of qualitative evidence surrounding the influences on decision-making regarding antipsychotic prescribing in nursing home residents with dementia, using a meta-ethnographic approach.

Chapter 5: A primary qualitative research study exploring the barriers and facilitators to appropriate antipsychotic prescribing in nursing home residents with dementia, using semi-structured interviews.

Chapter 6: A methodological study describing the development of a complex intervention using the BCW approach and informed by PPI.

Chapter 7: A mixed-methods feasibility study of the newly developed complex intervention in an Irish nursing home setting.

Chapter 8: An overall discussion of the research, including strengths and limitations with suggestions for future research and implications for policy and practice.

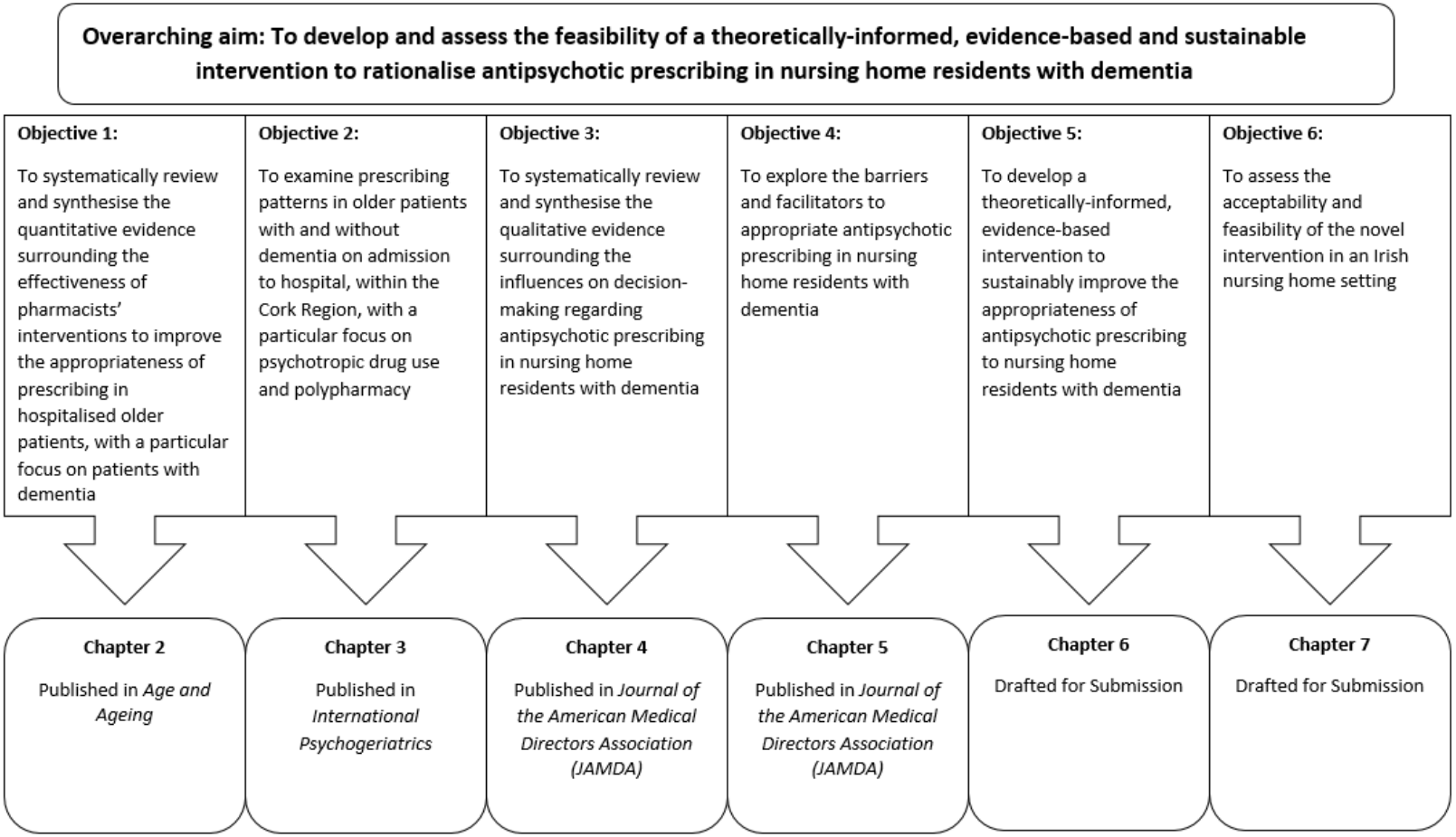


Figure 9: Thesis outline (Objectives and Outputs)

Chapter 2. Improving the Appropriateness of Prescribing in Older Patients: A Systematic Review and Meta-Analysis of Pharmacists' Interventions in Secondary Care

2.1 Chapter Description

In Chapter 1, I explained how people with dementia are particularly vulnerable to the adverse effects of certain medications, and how pharmacists as part of interdisciplinary teams have been found to be effective in reducing inappropriate prescribing to this cohort, in certain settings. In this chapter, I examine the effectiveness of pharmacists' interventions in improving the appropriateness of prescribing in older hospitalised adults, with a particular focus on those with dementia. An addendum is provided at the end of this chapter with a discussion of up-to-date search results.

The work of this chapter has been published as: *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 Jan 10; 45(2):201-9.* (1)

2.2 Abstract

2.2.1 Introduction

PIP in older hospitalised patients, and in particular those with dementia, is associated with poorer health outcomes. PIP reduction is therefore essential in this population.

2.2.2 Methods

We conducted a comprehensive electronic literature search using twelve databases from inception up to and including September 2014. Inclusion criteria were controlled trials (randomised or non-randomised) of interventions involving pharmacists conducted in hospitals, with an objective of the study being PIP reduction in patients 65 years or older, or patients with dementia of any age, using any validated PIP tool as an outcome measure. We conducted risk of bias assessments utilising the Cochrane Risk of Bias Tool.

2.2.3 Results

A total of 1,752 records were found after duplicates were removed. Four trials (n = 1,164 patients; two randomised, two non-randomised) from three countries were included in the quantitative analysis. All studies were at moderate risk of bias. No study focused specifically on dementia patients. Three trials reported statistically significant reductions in the Medication Appropriateness Index (MAI) score in the intervention group (mean difference from admission to discharge = -7.45, 95% CI: -11.14, -3.76) and other PIP tools such as Beers Criteria. One trial reported reduced drug-related readmissions and another reported increased adverse drug reactions.

2.2.4 Conclusion

Multi-disciplinary teams involving pharmacists may improve prescribing appropriateness in older inpatients, though the clinical significance of observed reductions is unclear. More research is required into the effectiveness of pharmacists' interventions in reducing PIP in dementia patients. Additionally, easily assessed and clinically relevant measures of PIP need to be developed.

2.3 Introduction

PIP is a universal term to describe various suboptimal prescribing practices, in particular the use of medicines where the risk associated with its use outweighs the potential benefits, especially when there are more effective alternatives available (178). PIP in older people is highly prevalent across a variety of healthcare settings and is associated with an increased risk of adverse drug events, morbidity, mortality and healthcare utilisation (179-183).

People with dementia are particularly vulnerable to the adverse effects of certain classes of medications (184). Of particular concern are anticholinergics (185, 186), antipsychotics (112, 187) and benzodiazepines (188, 189) which are known to cause considerable harm to this population if prescribed inappropriately e.g. increased risk of falls, stroke and mortality. Reduction of PIP is therefore of critical importance in this population (190).

Clinical pharmacists are suitably trained to carry out medication reviews in older patients and have been found to improve the appropriateness of prescribing in different settings (191-194). However, a European-wide survey of hospital pharmacists reported that only 6% of hospital pharmacies perform decentralised clinical services (whereby pharmacists work at least 50% of the time on the ward) (195). This suggests that clinical services provided by hospital pharmacists are still quite limited in Europe. This is in contrast to the United States where this model of care is widely implemented (196).

Our primary objective for this review was to collate all the available evidence on the effectiveness of pharmacist interventions on the quality of prescribing among older hospitalised patients. A secondary objective of our review was to undertake a parallel meta-analysis specifically among hospitalised patients of any age with dementia.

2.4 Methods

2.4.1 Search Strategy and Selection Criteria

2.4.1.1 Search Strategy

We conducted this systematic review and meta-analysis in compliance with *'Preferred Reporting Items for Systematic Reviews and Meta-Analyses'* (PRISMA) guidelines (197). We conducted an electronic search of the literature using the following twelve electronic databases from inception up to and including June 2014; Medline (through OVID), PubMed, EMBASE, Centre for reviews and dissemination databases, Cochrane database of systematic reviews, CINAHL, Web of Science, Science Direct, ClinicalTrials.gov, *meta*Register of Controlled Trials, ProQuest Dissertations and Theses, and Index to Theses in Great Britain and Ireland. We updated the search in September 2014.

We designed the search strategy in Medline (through OVID) using a combination of important key words and Medical Subject Headings (Appendix 1). Using one key paper that was known *a priori* as being eligible for inclusion (198), we adapted the search strategy to suit the specific search capabilities of each of the remaining databases to ensure that it was sensitive enough to at least detect this paper. This approach was utilised in order to be as sensitive as possible due to the anticipated

limited number of potentially relevant studies. For example in PubMed, the search terms included synonyms and various combinations of the following key words; “pharmacist” AND “inappropriate prescribing” AND (“older people” OR “dementia”) AND “hospital” AND “pharmaceutical care”. However this differed for Medline (OVID) where the search terms included synonyms and combinations of the following key words (“older people” OR “dementia”) AND “inappropriate prescribing” AND “hospital”. Although the search strategy was adapted for each database, we attempted to utilise the PICO framework where possible for each database (i.e. population, intervention, comparator and outcome). However there have been some limitations reported in the literature with using the PICO framework (199), hence we decided upon advice from the medical librarian to use variations of this framework (200), with the aim of being sensitive enough to detect one particular study at the very least from each database (198).

Additionally, we utilised other methods including hand-searching key journals and conference proceedings, citation searching of highly cited key papers, scanning reference lists of key papers and by contacting experts in the field.

2.4.1.2 Eligibility criteria

Inclusion criteria were controlled trials of interventions (randomised controlled trials, non-randomised controlled trials or controlled before-after studies) involving pharmacists conducted in hospitals, in which an objective of the study (either primary or secondary) was the reduction of PIP in patients 65 years or older, or patients of any age with dementia, using any validated PIP tool as an outcome measure.

As determined *a priori*, we included studies involving patients younger than 65 years old if the effectiveness in older and younger people could be clearly separated, or if the studies looked specifically at people with dementia due to the fact that a certain proportion may have young-onset dementia (201). Trials which were conducted across transitions of care were only included if there was a clear delineation between the inpatient and outpatient settings in terms of the population, intervention, comparator and outcomes. Additionally the inpatient intervention must have occurred first. Only the data in relation to the inpatient setting were extracted.

Examples of validated PIP tools include STOPP/START (202), Beers Criteria (203) and MAI (204). Explicit criteria (e.g. STOPP/START and Beers Criteria) contain specific clinical and drug recommendations that can reduce PIP in older patients. Implicit criteria (e.g. MAI) refer to quality indicators of prescribing that can be applied to prescriptions and require professional judgement (205).

There was no language exclusion initially. Potentially relevant foreign language articles were only excluded once the authors confirmed there were no English versions available. We contacted authors of potentially relevant studies published in conference abstracts, Masters Theses and on-going clinical trials to determine whether the study had been published in full in a peer-reviewed journal or a PhD thesis. Hence Masters Theses and ongoing clinical trials were excluded.

2.4.1.3 Study selection

For the first stage of study selection, two reviewers independently screened titles and abstracts to identify potentially relevant papers. In the second stage, two reviewers independently reviewed the full texts of papers. Consensus on inclusion in

both stages was reached by discussion between reviewers, with arbitration by a senior supervisor if necessary.

2.4.2 Data Extraction

Data extraction were performed by one reviewer and verified by another. Authors of the primary studies were contacted at this stage if vital data were missing.

2.4.3 Risk of Bias Assessments

Risk of bias assessments were conducted by two independent reviewers utilising the Cochrane Collaboration's tool (206). We piloted the tool on two of the five papers initially and as a result it was modified by consensus as follows: objective and subjective outcomes were separated, as the main outcome of interest (MAI) is a subjective outcome. The 'other bias' domain dealt with issues that did not fit into other domains e.g. contamination bias. Using this tool, the nine domains were deemed to have a low, high or unclear risk of bias. Consensus on the assessments was reached by discussion, with arbitration by a senior supervisor if necessary.

2.4.4 Data Synthesis

We performed quantitative analysis where there was a common comparable outcome in at least three included studies and combining results in this manner was considered appropriate. For the two continuous outcomes of interest, (a) the summated MAI scores per patient at discharge and (b) the change in summated MAI scores per patient from admission to discharge, we performed fixed or random effects meta-analyses depending on the degree of statistical heterogeneity as estimated by the I^2 statistic. The summated MAI score is reported as a continuous

variable (0 to 18 per medication) with higher scores inferring more inappropriate prescribing (204).

Following previous convention in a Cochrane review of a related topic, if clinical heterogeneity was apparent or if substantial/considerable statistical heterogeneity was observed (I^2 > 50% or if Chi^2 < 0.1), we analysed the data using the random-effects model (207). The random-effects model assumes that the varying effect sizes underlying different studies are drawn from a normal distribution. Studies in health services research are likely to have numerous differences in terms of population, intervention and outcome, such that a common effect size is not seen and thus heterogeneity is assumed. In trials where the effects are assumed to be different, but similar, a random-effects model can be utilised to reflect this similarity (208).

We utilised Review Manager 5.3 to create overall summary estimates of effects (209). The continuous data were presented as the mean differences with their 95% CI. Clinical outcomes such as mortality, Emergency Department (ED) visits, hospital re-admissions and adverse drug reactions (ADRs), and all other PIP criteria outcomes were interpreted as a narrative synthesis.

2.5 Results

2.5.1 Search Results

We found a total of 1,752 unique records after duplicates were removed from electronic database searching (n = 1,940) and other sources (n = 185) (**Figure 10**). After the exclusion of records based on their title and abstracts (n = 1,731) there were 21 papers suitable for full text review. No foreign language article was found to be

eligible. Five papers were eligible for inclusion in the final review (198, 210-213). Only four of these papers were included in the meta-analysis, as we considered one paper to have an unacceptably high risk of bias as we agreed that addition of this biased study could falsely skew the overall results (210). However we conducted sensitivity analyses to assess the impact of including and excluding this study (**Figure 14** and **Figure 15** below).

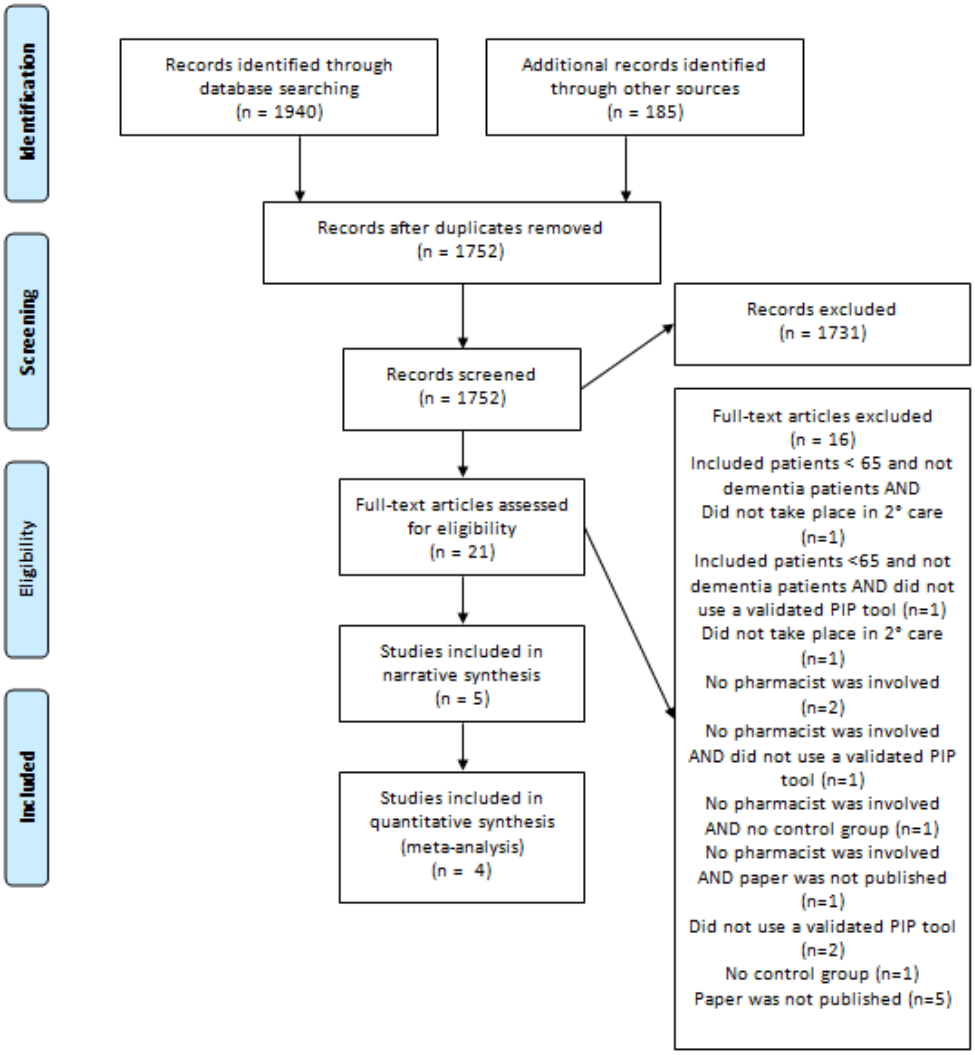


Figure 10: PRISMA flow diagram of search strategy results.

2.5.2 Characteristics of Included Trials

The characteristics and outcomes of the five included trials are summarised in **Table 1**. No trial specifically studied patients with dementia; therefore the secondary objective of this review could not be undertaken.

One included trial was conducted between primary and secondary care settings. Additionally, the appropriateness of prescribing was a secondary outcome in this trial, and the primary authors only assessed a random sample of 400 patients for this outcome out of 834 total patients (**Table 1**).

In three trials, the intervention comprised of the addition of a clinical pharmacist to the already existing ward-level healthcare team (198, 210, 211). The other two trials involved interventions conducted by a newly formed multi-disciplinary team, which included a clinical pharmacist (212, 213). The various components of the multi-disciplinary teams, the speciality of the physicians involved and the activities undertaken by the pharmacists are detailed in **Table 2**.

Several prescribing criteria to evaluate appropriateness of prescribing in older patients were utilised in these trials, MAI (198, 210-213), STOPP/START (211), Beers criteria (198, 213), Assessment Of Underutilisation of medication (AOU) (213) and Assessing Care Of Vulnerable Elders (ACOVE) (198). Data from the MAI criteria are reported in **Table 1** and **Figure 13**, with data from the other criteria reported in **Table 3**

2.5.3 Results of the Risk of Bias Assessments

The results of the Cochrane Risk of Bias tool assessments are presented in **Figure 11** and **Figure 12**.

Table 1: Study design, characteristics and outcomes of the included studies.

Author and Year	Country	Setting	Study Design	Aim of study	No. of patients	Mean age in years ±S.D	% Male	Mean no. of Rx meds per patient ± S.D	Inclusion of dementia patients	% Dementia	Mean Summated MAI score per patient at baseline ±S.D	Mean Summated MAI score per patient at discharge ±S.D	Number of ADRs (events per 1000 days)	% Patients re-admitted post-discharge	% Patients who had ED visit before close out of trial	% Patients with a drug-related revisit to hospital	% Patients who died before close-out of trial
Bergkvist (2009) (210)	Sweden	Three internal medicine wards in a university hospital	NRCT	To evaluate if an integrated medicines management programme can improve the appropriateness of drug use in the elderly	I: 28 C: 25	I: 82 ± 6 C: 84 ± 6	I: 39% C: 36%	I: 7.9 ± 3.4 C: 8.3 ± 4.4	Yes	NR	I: 11.5 ± 12.4 C: 18.8 ± 12.9*	I: 6.36 ± 10.3 C: 17.5 ± 15.0*					
Gillespie (2013) (211)	Sweden	Two internal medicine wards in a university hospital	RCT	To investigate the effects of pharmacists' interventions on appropriateness of prescribing in elderly patients	I: 182 C: 186	I: 86.4 ± 4.2 C: 87.1 ± 4.1	I: 42.3% C: 40.3%	I: 8.7 ± 4.5 C: 7.3 ± 4.4	Yes	I: 11.0% C: 14.5%	I: 8.5 ± 6.8 C: 8.7 ± 7.3	I: 5.0 ± 4.2 C: 10.0 ± 7.3		I: 58.2 C: 59.1°	I: 49 (0.35) C: 93 (0.66)**	I: 9 (0.06) C: 45 (0.32)**	I: 31.3 C: 32.8 °
Hellstrom (2011) (212)	Sweden	Three internal medicine wards in a university hospital	NRCT	To examine the impact of systematic medication reconciliations upon hospital admission and of a medication review on the number of inappropriate medications and unscheduled drug-related hospital revisits in elderly patients	I: 109 C: 101	I: 83.0 ± 7.0 C: 81.8 ± 7.4	I: 45% C: 49.5%	I: 8.1 ± 4.2 C: 8.0 ± 4.0	Yes	NR	I: 12.5 ± 13.05 C: 10.8 ± 10.88	I: 4.5 ± 7.99 C: 4.9 ± 7.25°				I: 5.6 C: 12.0°	
Schmader (2004) (213)	USA	Eleven Veteran Affairs Medical Centres	RCT	To determine if inpatient or outpatient geriatric evaluation and	I: 430 (202 for secondary outcomes)	I: 46% (65-73 years)	I: 97% C: 98%	I: 7.7 ± 3.6 C: 7.6 ± 3.7	Yes but severe dementia patients	NR	I: 10.0 ± 7.8 C: 7.7 ± 7.2	I: 5.3 ± 4.9 C: 9.6 ± 8.2	I: 20.5 C: 11.2*				

				management, as compared with usual care, reduces adverse drug reactions and suboptimal prescribing in frail elderly patients.	C: 404 (198 for secondary outcomes)	54% (≥ 74 years) C: 47% (65-73 years) 53% (≥ 74 years)			excluded								
Spinewine (2007) (198)	Belgium	Acute Geriatric Evaluation and Management Unit of a university hospital	RCT	To evaluate the effect of pharmaceutical care provided in addition to acute geriatric evaluation and management care on the appropriateness of prescribing	I: 96 C: 90	I: 82.4 ± 6.9 C: 81.9 ± 6.2	I: 28.1% C: 33.3%	I: 7.9 ± 3.5 C: 7.3 ± 3.3	Yes	I: 43.8%^ C: 46.7%^	I: 24.1 ± 17 C: 21.2 ± 14.3	I: 7.1 ± 7.5 C: 19.3 ± 12.5		I: 32.6 C: 33.7°	I: 7.9 C: 12.0°		I: 22.5 C: 30.1°

*No., numbers; S.D, standard deviation; Rx, prescription; I, intervention group; C, control group; RCT, randomised controlled trial; NRCT, Non-randomised controlled trial; ^value included patients with a diagnosis of dementia or the identification of cognitive problems without dementia; MAI, medication appropriateness index; ADRs, adverse drug reactions; ED, emergency department; * Statistically significant difference between intervention and control group where P < 0.05; ° No statistically significant difference found between intervention and control groups where P ≥ 0.05; ** Statistically significant difference between intervention and control group using quotient as a comparison where 95% CI does not cross 1.0. NR, reviewers asked primary authors for this information however it was Not Recorded.*

Note blank spaces refer to data that were not reported by the primary authors and reviewers did not seek this information.

Table 2: Criteria applied, skill mix and Pharmacists' access/activity in intervention groups.

Author and Year	Criteria Applied	List of health care professionals involved	Speciality of Physician	Access to medical notes?	Access to lab data?	Patient/ Caregiver Interview undertaken?	Med Rec carried out?	Patient counselling undertaken?	Chart review carried out?	Routine Participati-on in ward rounds?	Geriatric Evaluation and Management structure?	Written communication with physicians?	Oral communication with physicians?	Participation in discharge planning?	Pharmaceutical Care post-discharge?
Bergkvist (2009) (210)	MAI	Pharmacists, physicians and nurses	Internal medicine	Yes	Unclear	Yes	Yes	Yes	Yes	No	No	Unclear	Yes	Yes	No
Gillespie (2013) (211)	MAI, STOPP, START	Pharmacists, physicians and nurses	Internal medicine	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Hellstrom (2011) (212)	MAI	Pharmacists, physicians, nurses, carers and paramedics	Internal medicine	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No
Schmader (2004) (213)	MAI, Beers, AOU	Geriatrician, nurses, social workers, pharmacists, dietitians, physio-therapists, occupational therapists.	Geriatric medicine	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	No	Yes	Unclear	Unclear	Unclear	Yes
Spinewine (2007) (198)	MAI, Beers, ACOVE	Pharmacists, geriatricians, nurses, physio-therapists, psychologist, occupational-therapist	Geriatric medicine	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

Med Rec, medicines reconciliation; MAI, medication appropriateness index; STOPP, screening tool of older persons' prescriptions; START, screening tool to alert doctors to right treatment; Beers, beers criteria; AOU, assessment of underutilisation of medication; ACOVE, assessing care of vulnerable elders.

Table 3: Changes in Appropriateness of Prescribing from Admission to Discharge utilising other Potentially Inappropriate Prescribing Criteria.

Study	No. of inappropriate drugs per patient according to Beers criteria at admission (mean ± S.D)	No. of inappropriate drugs per patient according to Beers criteria at discharge (mean ± S.D)	No. of inappropriate drugs per patient according to STOPP criteria at admission (mean ± S.D)	No. of inappropriate drugs per patient according to STOPP criteria at discharge (mean ± S.D)	No. of omitted drugs per patient according to START criteria at admission (mean ± S.D)	No. of omitted drugs per patient according to START criteria at discharge (mean ± S.D)	No. of omitted drugs per patient according to AOU criteria at admission (mean ± S.D)	No. of omitted drugs per patient according to AOU criteria at discharge (mean ± S.D)	No. of inappropriate ratings per patient according to ACOVE criteria at admission (mean ± S.D)	No. of inappropriate ratings per patient according to ACOVE criteria at discharge (mean ± S.D)
Bergkvist (2009) (210)										
Gillespie (2013) (211)			I: 1.4 ± 1.5 C: 1.5 ± 1.5	I: 0.9 ± 1.0 C: 1.7 ± 1.5*	I: 0.4 ± 0.7 C: 0.4 ± 0.7	I: 0.1 ± 0.3 C: 0.5 ± 0.7*				
Hellstrom (2011) (212)										
Schmader (2004) (213)	I: 0.5 ± 0.7 C: 0.5 ± 0.7	I: 0.2 ± 0.5 C: 0.4 ± 0.6 *					I: 1.4 ± 1.3 C: 1.0 ± 1.1	I: 1.0 ± 1.1 C: 1.1 ± 1.3*		
Spinewine (2007) (198)	I: 0.29 ± 0.56 C: 0.44 ± 0.69	I: 0.03 ± 0.17 C: 0.04 ± 0.21*							I: 0.75 ± 0.89 C: 0.92 ± 0.95	I: 0.17 ± 0.43 C: 0.63 ± 0.81*

*No., number; I, S.D, standard deviation; intervention group; C, control group; STOPP, screening tool of older persons' prescriptions; START, screening tool to alert doctors to right treatment; Beers, beers criteria; AOU, assessment of underutilisation of medication; ACOVE, assessing care of vulnerable elders; *Statistically significant difference between intervention and control groups where p <0.05. Note that blank fields indicate that this information was not reported by the authors. Authors were not contacted for this additional information as they were considered unlikely to have used all of the other PIP criteria.*

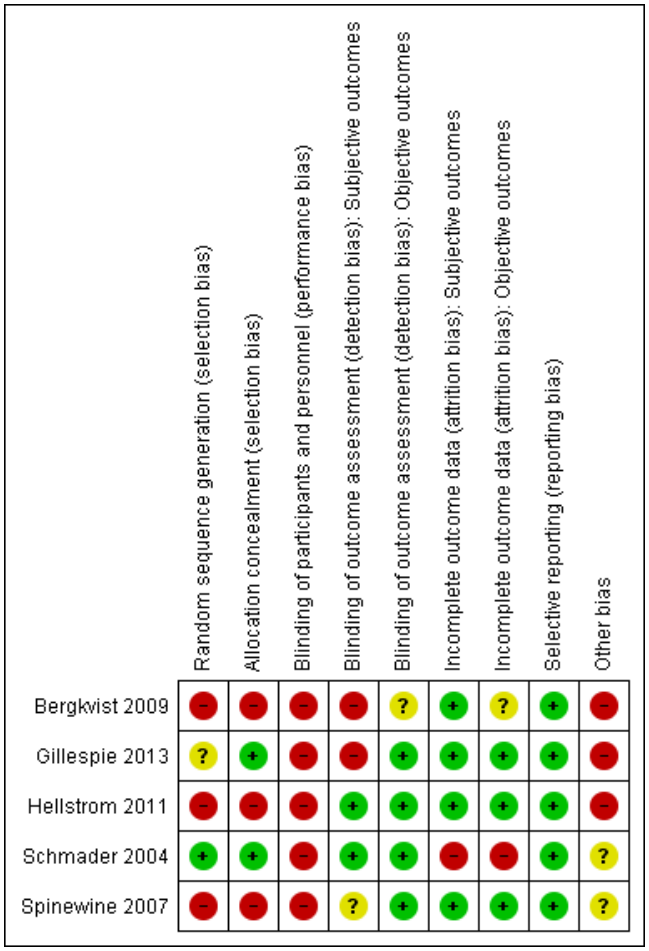


Figure 11: Risk of bias assessments.

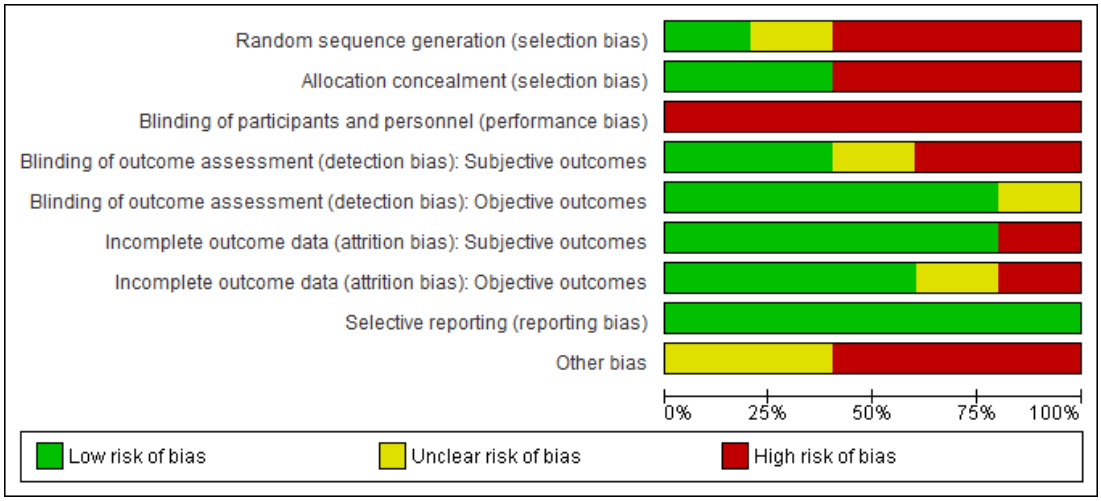


Figure 12: Review authors' judgements about each risk of bias item presented as percentages across all five included studies

Overall, we assessed the five included studies to have a moderate to high risk of bias (206). We determined one study in particular to be at a high risk of bias (210). As such the confidence in the results of this trial is seriously weakened and in order to preserve the quality of evidence in the meta-analysis, we decided by consensus to exclude this trial from the quantitative analysis. We performed a sensitivity analysis and we determined that removal of this study did not impact on the findings (**Figure 14** and **Figure 15**).

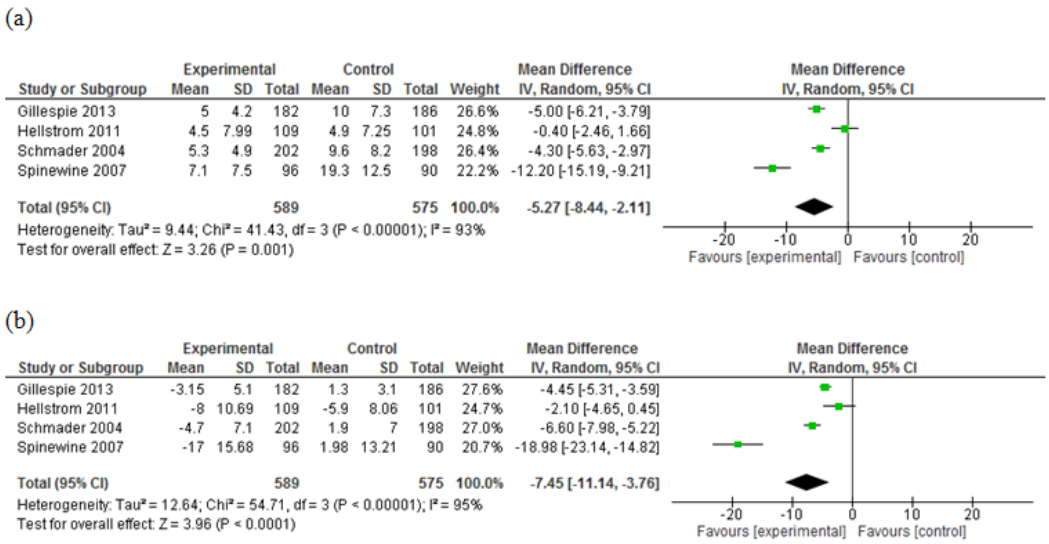


Figure 13(a). Forest plots of comparison: Summated MAI scores at discharge.
Figure 13(b). Change in summated MAI scores from admission to discharge.

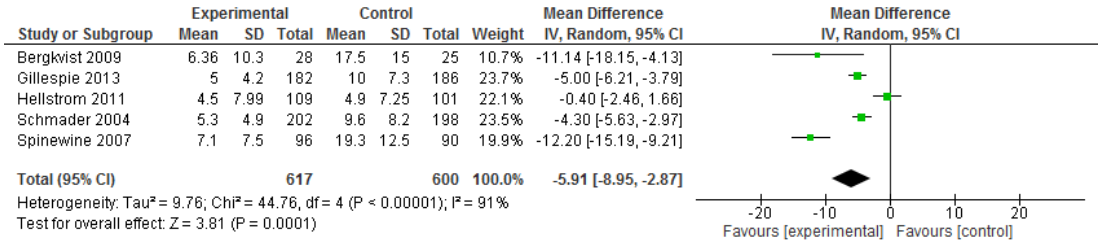


Figure 14: Sensitivity Analysis: Summated MAI score at discharge <u>including</u> study at high risk of bias.

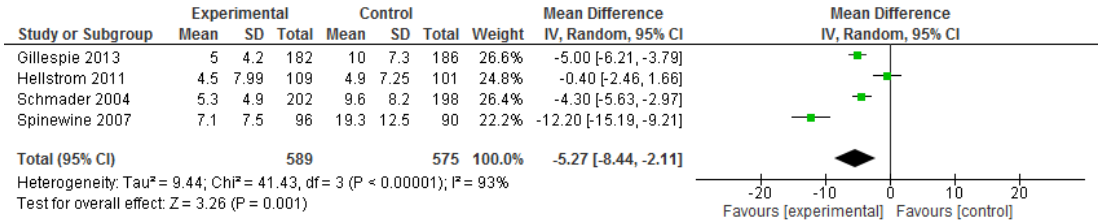


Figure 15: Sensitivity Analysis: Summated MAI score at discharge <u>excluding</u> study at high risk of bias.

We found the blinding of subjective outcome assessments to have an unclear or high risk of bias in three of the studies (198, 210, 211) (**Figure 12**). As MAI is a subjective outcome, it is important to consider the potential impact that bias in this domain may have on the overall result.

2.5.4 Quantitative Analysis

In the four trials included, there were a total of 1,164 patients (589 and 575 in the intervention and control arms respectively). The mean number of prescribed medications and the standard deviations were 8.1 ± 4.0 and 7.5 ± 3.9 in the intervention and control arms respectively. Summated MAI scores per person were reported as an outcome in all four trials and so were amenable to quantitative analysis (**Table 1**). MAI scores at baseline ranged greatly both within and between

trials (0-35 in one trial (211) and 0-64 in another (212)). This information was not reported by the other trials, however it is evident from the variation in the mean and standard deviations of the MAI scores at baseline that the range differed greatly between trials (**Table 1**).

The intervention resulted in a reduction in MAI score at discharge (n=4, mean difference in MAI score = -5.27, 95% CI: -8.44, -2.11). Similarly, the intervention resulted in a reduction in MAI score, when the changes from baseline data were analysed (n=4, mean difference in MAI score = -7.45, 95% CI: -11.14, -3.76) (**Figure 13**).

We identified considerable statistical heterogeneity among these trials with I^2 values of 93% and 95% determined for **Figure 13(a)** and **Figure 13(b)** respectively. We performed a random-effects model to address heterogeneity among studies.

2.5.5 Clinical Outcomes

Overall the interventions had varying effects on other outcomes (**Table 1**). Two trials failed to show any statistically significant difference in mortality and hospital re-admission, however neither were powered to look at these outcomes (198, 211). One of these trials did show significant reductions in both ED visits and drug-related readmissions (211). In one trial, ADRs were detected significantly more frequently in the intervention group **(Table 1)** (213). The authors of this study hypothesised that this was due to the increased knowledge and awareness of the intervention team.

2.6 Discussion

Our systematic review and meta-analysis shows that multi-disciplinary patient care teams involving pharmacists may improve the appropriateness of prescribing in older hospitalised patients. We calculated an overall reduction in the mean MAI score per patient of 7.45 in the intervention group. However, the clinical significance of such an MAI score reduction is unclear. In a study set in a primary care setting in the US higher MAI scores were associated with an increased number of ED visits (although the relationship was found to be non-significant) (214). Additionally, in a study conducted in a hospital setting in Belgium, higher MAI scores were significantly associated with drug-related hospital admissions (215) (216). However an association between MAI scores and mortality or total hospital admissions has not yet been proven. It must be noted that the two included studies reporting mortality and admission outcomes were not adequately powered to detect any differences. Given its unclear clinical significance and subjective assessment, MAI score improvements should be viewed with caution.

Furthermore, one of the studies found that ADRs were detected significantly more frequently in the intervention compared to the control group (213). The authors of this study speculated that this was due to the increased knowledge and awareness of the intervention team as a result of the training. However it is also possible that ADRs occurred more frequently as a result of the intervention pharmacists' recommendations to withdraw or initiate medication.

This positive association between pharmaceutical care of older patients and appropriate prescribing has been determined previously in several reviews (207, 217-

222). The mechanism of this improvement may be due to a combination of aspects such as medicines reconciliations, medication reviews and in particular, working as part of a multi-disciplinary team (196, 207, 217-220, 222-225).

A secondary objective of this review was to collate all the available evidence on the effectiveness of pharmacists' interventions on the appropriateness of prescribing in hospitalised dementia patients. From the exhaustive search of the literature we concluded that no such trial had been carried out by pharmacists, as of yet. Two interventional studies involving interdisciplinary geriatric and psychiatric care teams were found which reported significant reductions in PIP in this population, but they did not involve a pharmacist (158, 226). As hospitalised dementia patients are particularly vulnerable to the adverse effects of PIP, it is crucial that more research is conducted in this area in order to help guide hospital policy and practice. Pharmaceutical care might improve the appropriateness of prescribing in dementia patients to a greater extent than the general older population, but even more likely it would improve clinical outcomes to a greater extent, given the particular risks of PIP in this group. Such information would thus guide healthcare management to target scarce pharmacy support to this vulnerable group.

The main strength of our systematic review was the comprehensive search strategy applied by us without language or date limitations. By complementing the electronic search with other manual search methods this ensured an exhaustive search. Furthermore, study selection and risk of bias assessments were performed by two independent reviewers with arbitration by a third party if necessary. This reduced

the risk of studies being omitted and also reduced the risk of selection bias entering the review process (227).

A limitation is that we found considerable statistical heterogeneity between included studies. Consequently the pooled estimates of effects should be viewed with caution. This heterogeneity may be a consequence of both clinical (variability of the interventions and patient characteristics) and methodological diversity (variability in the blinding of subjective outcomes and allocation concealment). There were too few studies included to adequately perform subgroup analyses to explore the heterogeneity. Some researchers argue that meta-analyses should only be undertaken when a group of studies is sufficiently homogenous; as conclusions are less clear when included studies have differing results (228, 229). In order to incorporate heterogeneity among the studies we decided that a random-effects model would be appropriate, as it allows the true effect size to vary from study to study (230).

Another limitation was that we found the trials to be at a moderate risk of bias and this may have impacted on the overall findings. Furthermore, as is common within complex interventions, it was difficult to ascertain the precise components that contributed to the intervention success. Future studies should be designed to mitigate this risk of bias by conducting adequate randomisation procedures and paying particular attention to blinding outcome assessors. They should also provide better reporting of the precise specifications of trial processes, including who exactly delivers the intervention and to whom (231).

It is important to note that the published literature is surprisingly limited in this area. Furthermore, we found that measuring PIP in a robust and clinically meaningful way is challenging, and we suggest that user-friendly PIP tools should be further developed to allow the effectiveness of interventions to be compared.

Despite these limitations, this study is useful for clinicians as it provides evidence that involvement of a pharmacist in the patient care team may reduce PIP, which is definitively linked to poorer outcomes, even if the included studies didn't prove better outcomes. More high quality research may be required to definitively prove better patient outcomes. Policy-makers have a key role to play in increasing the number of pharmacists in multi-disciplinary patient care teams (232). Creation of more clinical-specialist pharmacist roles as opposed to drug-distribution roles, by greater use of automation in the dispensary, is one strategy which may permit pharmacists to have adequate time to perform clinical duties and to take on more multi-disciplinary patient care roles (233, 234).

2.7 Conclusion

Pharmacists may improve the appropriateness of prescribing in older hospitalised patients when they work as part of a team. However in light of the moderate risk of bias, subjective nature of MAI assessments and high heterogeneity, these results should be viewed with caution. Moreover, PIP tools should be further developed to permit better assessment of the effectiveness of interventions. More research is required to determine the effectiveness of pharmacists' interventions in hospitalised dementia patients. In order to develop such interventions a greater understanding of the unique pharmaceutical care needs of dementia patients is required. This can

be achieved through additional quantitative (e.g. examining prescribing patterns) and qualitative research (e.g. exploring barriers and facilitators to changing healthcare professionals' prescribing behaviours).

2.8 Addendum

2.8.1 Updated Search Results

An updated search of the electronic databases was conducted on July 2nd 2018, to search for all potentially relevant articles published since September 2014 (date of latest search prior to publication). A total of 1,473 records were identified. After duplicate removal 1,024 records were screened by title and abstract and 25 full-text articles were subsequently assessed for eligibility. This resulted in five articles meeting our inclusion criteria and hence were included in our updated search (235-239) (**Figure 16**).

2.8.2 Analysis Methods

Due to the heterogeneity of outcome measures reported, only one of the five new articles could be included in the updated meta-analysis (235) (**Figure 17**). Therefore a narrative synthesis of all five new studies, and an updated quantitative synthesis including one additional study was conducted.

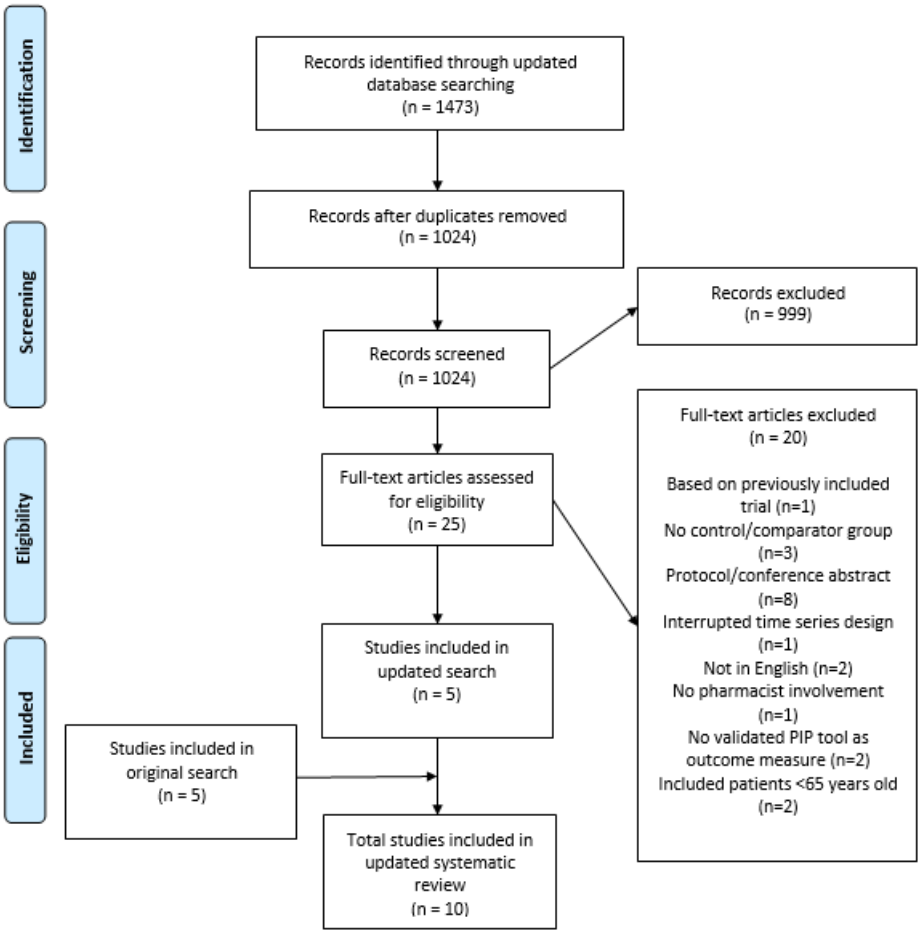
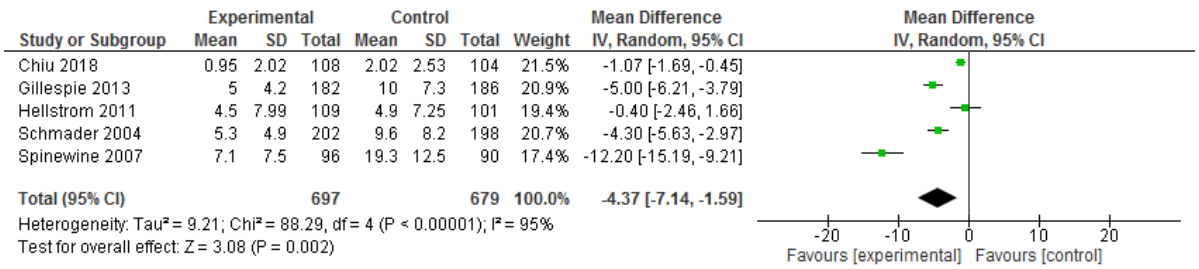


Figure 16: PRISMA flow diagram of updated search strategy results.



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Chiu 2018	0.95	2.02	108	2.02	2.53	104	21.5%	-1.07 [-1.69, -0.45]
Gillespie 2013	5	4.2	182	10	7.3	186	20.9%	-5.00 [-6.21, -3.79]
Hellstrom 2011	4.5	7.99	109	4.9	7.25	101	19.4%	-0.40 [-2.46, 1.66]
Schmader 2004	5.3	4.9	202	9.6	8.2	198	20.7%	-4.30 [-5.63, -2.97]
Spinewine 2007	7.1	7.5	96	19.3	12.5	90	17.4%	-12.20 [-15.19, -9.21]
Total (95% CI)			**697**			**679**	**100.0%**	**-4.37 [-7.14, -1.59]**

Heterogeneity: Tau² = 9.21; Chi² = 88.29, df = 4 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.08 (P = 0.002)

Figure 17: Forest plots of comparison: Updated Summated MAI scores at discharge.

2.8.3 Updated Narrative Synthesis and Meta-Analysis

Chiu *et al.* conducted a non-randomised, controlled trial (NRCT) in a geriatric unit of a regional hospital in Hong Kong (235). Two hundred and twelve patients ≥ 65 years old, were allocated to either routine care (n=104) if they were admitted on Friday through Sunday, or to the pharmacist intervention (n=108) if they were admitted on Monday through Thursday. The pharmacist intervention involved medicines reconciliation, medication review, and medication counselling. The control group did not receive pharmaceutical care. Recommendations made by the pharmacist were communicated to physicians in written and oral formats. The intervention improved medication appropriateness as determined by the MAI tool (applied by the intervention pharmacist), as the summated MAI score was significantly lower in the intervention group compared to control group at discharge (0.95 ± 2.02 vs. 2.02 ± 2.53, p <0.001) (**Figure 17**). Furthermore, unplanned hospital readmissions were significantly lower in the intervention group compared to control, one month after discharge (13.2% vs. 29.1%, p = 0.005). However, the difference in unplanned hospital readmissions became non-significant at three months (36.8% v 48.5%, p =0.086). Moreover there were no differences in the length of stay (p = 0.888), number of ED visits (p=0.079), or mortality rates (p = 1.000) between the two groups.

In an RCT conducted in Canada by Cossette *et al.*, 247 patients ≥ 65 years old, with at least one potentially inappropriate medicine (PIM) according to either Beers (203) or STOPP (68) criteria, were randomly allocated to receive either usual care or the intervention, upon admission to one of the participating university hospitals (237). As randomisation was conducted by hospitalisation episode, a patient could be

included in both control and intervention groups during different admissions. Furthermore, the same patient could be captured multiple times within the same group if there was multiple admissions during the study period. Hence for these 247 patients, 139 hospitalisations were randomised to the intervention group and 133 hospitalisations were randomised to the control group. The intervention consisted of computerised alerts of PIMs, along with assessment of these alerts for clinical relevance by pharmacists, and subsequent development of a therapeutic plan to reduce PIM use with the attending physician. Control group hospitalisations did not receive computerised alerts or the collaborative pharmacist-physician follow up. At discharge, there were significantly more PIM cessations or reduced dosages in the intervention group compared to control (48.1% vs. 27.3%; absolute difference 20.8%; 95% CI 4.6 – 37.0%). However there were no significant differences between the two groups in terms of length of stay ($p = 0.9$), in-hospital mortality ($p = 0.3$), ED visits ($p = 1.0$) or re-admissions ($p = 0.3$).

In Belgium, a NRCT was conducted by Van der Linden *et al.* investigating the effectiveness of a pharmacist intervention in improving the quality of prescribing and clinical outcomes, in 214 patients ≥ 65 years old admitted to acute geriatric wards (239). Allocation to the intervention (n=117) or control group (n=97) was based on whether the patient was admitted to the control ward or one of the two intervention wards. The intervention consisted of medicines reconciliation along with medication review based on the RASP (Rationalisation of home medication by an Adjusted STOPP in older Patients) list of PIMs (240). This intervention was conducted by the study pharmacists. The control group did not receive pharmaceutical care. At discharge, more PIMs were discontinued in the intervention group compared to control

[median (Interquartile range [IQR]) = 2 (1-3) vs. 0.5 (0-1); p <0.001]. Furthermore, the intervention was associated with a statistically (but not clinically) significant improved in quality of life measured using the EQ-5D-3L (+0.064 points, p = 0.008). However no differences were found between the two groups with regards any other clinical outcomes (e.g. mortality [p = 1.000], delirium [p = 1.000], inpatient falls [p = 0.520], outpatient falls [p=1.000], readmissions [p = 0.629], ED visits [p = 0.189]), except for the number of ED visits without hospital admission, which favoured the intervention group (8.9% in control vs. 1.1% in intervention, p = 0.021).

An Australian NRCT conducted by Mulvogue *et al.,* examined the effect of the addition of a clinical pharmacist to a physician-led geriatric ward round, on the quality of prescribing for inpatients ≥ 65 years old (238). In the comparator group, which occurred pre-intervention, there was a total of 96 patients. In the intervention group, there was a total of 100 patients. During the comparator study period, there was no pharmacist on the ward round and during the intervention study period, there was a pharmacist involved in twice-weekly physician-led ward rounds. Inappropriate prescribing as measured by the mean number of STOPP/START criteria per patient (202), was lower in the intervention group compared to comparator group at discharge, but not significantly so (1.18 ± 1.37 vs. 1.50 ±1.41; p=0.07). The impact on clinical outcomes was not measured in this study.

Finally, Najjar *et al.* conducted a NRCT in Saudi Arabia assessing the effectiveness of an educational and clinical pharmacist intervention in reducing the incidence of PIMs (as measured by Beers (203) and STOPP criteria (68)) among hospitalised patients ≥ 65 years old (236). Four hundred patients were enrolled in this study, 200 in the

comparator group (pre-intervention period) and 200 in the intervention group. The education component, which consisted of four 1-hour long sessions and the provision of written material, which was developed and delivered by a geriatrician and clinical pharmacists aimed to improved physicians' knowledge of updated evidence-based guidelines for prescribing in older people. The clinical pharmacist intervention component involved increased collaboration (e.g. audit and feedback, ward round participation) between the pharmacists and prescribers with the aim of utilising STOPP and Beers criteria to optimise prescribing. It is not clear what level of pharmaceutical care was delivered during the comparator period. As a result of the intervention, the *incidence* rate of PIMs was significantly lower in the intervention group compared to the comparator group (29.5% vs. 61%; $p<0.001$). However the *prevalence* of PIMs on admission and discharge for both groups was not reported. The impact on clinical outcomes was not assessed in this study.

2.8.4 Discussion

In total, five additional studies were found which all reported an improvement in the appropriateness of prescribing for older hospitalised patients as a result of pharmacists' interventions. Four out of five reported that these improvements were statistically significant in favour of the intervention group. We can see that the addition of Chiu *et al*. to the forest plot in **Figure 17**, did not significantly change the direction or magnitude of the effect size compared to the original forest plot (**Figure 13(a)**) (-4.37; 95% CI: -7.14, -1.59 vs. -5.27; 95% CI: -8.44, -2.11). Hence, the findings from these newer studies are in line with our originally included studies.

However, the interventions did not appear to have impacted on any of the clinical outcomes reported, except quality of life and the number of ED visits without hospital admission in one study (239), and unplanned hospital readmissions at one-month in another study (235). This apparent limited effect on clinical outcomes is in line with our initial findings, as well as another seminal systematic review (241). The possible reason behind these consistently non-significant impacts on clinical outcomes, particularly with regards mortality, is that the influences on these outcomes are often multifactorial and are not necessarily directly related to PIP (242), although associations have been reported (183). The recently published OPTIMIST RCT conducted in Denmark, which recruited over 1,400 hospitalised patients with polypharmacy (over the age of 18), found that the multifaceted pharmacist intervention significantly reduced the number of hospital readmissions and ED visits compared to usual care (243). However this intervention, similar to our findings, did not have any significant impact on mortality.

Once again, no study focused specifically on dementia patients, nor was any specific sub-group analysis conducted on this patient group. This is disappointing considering how vulnerable patients with dementia are to the adverse effects of certain medications (244), as well as the high prevalence of PIP and polypharmacy in hospitalised patients with dementia (245). Research is urgently required to determine the effectiveness of pharmacists' intervention in this area.

Due to time constraints, the searches and data extraction for this updated review, were conducted solely by the primary researcher. Furthermore, no grey literature searching and no risk of bias assessments were conducted, for this updated search.

Hence it is possible that important studies were unintentionally omitted from this updated search. Furthermore, there were some methodological concerns with the included studies, however these have not been quantified utilising any standardised risk of bias tool. Therefore I recommend that an updated systematic review be conducted, involving multiple reviewers, prior to dissemination of the updated findings.

Chapter 3. Patterns of Psychotropic Prescribing and Polypharmacy in Older Hospitalised Patients in Ireland: A Retrospective Cross-Sectional Study

3.1 Chapter Description

In Chapter 2, I conducted a systematic review and meta-analysis, and the findings showed that pharmacists' interventions in hospital settings were effective at reducing PIP in older hospitalised patients. However I found no intervention aimed at improving the quality of prescribing specifically in hospitalised patients with dementia. In this chapter, I investigate whether there are any differences between older patients with and without dementia on admission to hospital, in terms of patterns of prescribing. Evidence from this study will help to identify divergence in these prescribing patterns and hence will suggest areas for future targeted interventions.

The work of this chapter has been published as: *Walsh KA, O'Regan NA, Byrne S, Browne J, Meagher DJ, Timmons S. Patterns of psychotropic prescribing and polypharmacy in older hospitalized patients in Ireland: the influence of dementia on prescribing. International Psychogeriatrics. 2016 Nov; 28(11):1807-20.* (2)

3.2 Abstract

3.2.1 Background

BPSD are ubiquitous in dementia and are often treated pharmacologically. The objectives of this study were to describe the use of psychotropic, anticholinergic and deliriogenic medications and to identify the prevalence of polypharmacy and psychotropic polypharmacy, among older hospitalised patients in Ireland, with and without dementia.

3.2.2 Methods

All older patients (≥ 70 years old) that had elective or emergency admissions to six Irish study hospitals were eligible for inclusion in a longitudinal observational study. Of 676 eligible patients, 598 patients (88% of total eligible patients) were recruited and diagnosed as having dementia, or not, by medical experts. These 598 patients were assessed for delirium, medication use, co-morbidity, functional ability and nutritional status. We conducted a retrospective cross-sectional analysis of medication data on admission for 583/598 patients with complete medication data (97.5% of those recruited), and controlled for age, sex and co-morbidity.

3.2.3 Results

Of 149 patients diagnosed with dementia, only 53 (35.5%) had a previous diagnosis. At hospital admission, 458 patients of the 583 included patients (78.6%) experienced polypharmacy (≥ 5 medications). The prevalence of polypharmacy (≥ 5 medications) was 84% (n=123) in people with dementia and 77% (n=335) in people without

dementia, however this difference was not significant (p=0.08). People with dementia were significantly more likely to be prescribed at least one psychotropic medication than patients without dementia [99/147 (67.4%) vs. 182/436 (41.7%); p<0.001]. People with dementia were also more likely to experience psychotropic polypharmacy (≥ two psychotropics) than those without dementia [54/147 (36.7%) vs. 61/436 (14%); p<0.001]. There were no significant differences in the prescribing patterns of anticholinergics [23/147 (15.7%) vs. 42/436 (9.6%); p=0.18] or deliriogenics [79/147 (53.7%) vs. 235/436 (53.9%); p=0.62]. Patients admitted from nursing homes were almost five times more likely to be prescribed an antipsychotic than those who were admitted from home controlling for dementia diagnosis, age, sex and co-morbidity (χ^2 = 26.7; aOR = 4.8; 95% CI = 1.9 - 12.1; p-value = 0.001).

3.2.4 Conclusion

Polypharmacy and psychotropic drug use is highly prevalent in older Irish patients on admission to hospital, especially in people with dementia. Hospital admission presents an opportunity for medication reviews in people with dementia, however interventions aimed at improving the appropriateness of antipsychotic prescribing in people with dementia may be more worthwhile if conducted in nursing home settings.

3.3 Introduction

The number of people with dementia is escalating worldwide; estimates project the prevalence at over 131.5 million by 2050 (25). The majority will experience BPSD, also referred to as NPS during their disease (246). BPSD refers to the spectrum of distressing, non-cognitive symptoms of dementia, ranging from wandering and agitation to delusional and aggressive behaviour (247). Psychotropic medications are commonly prescribed to manage BPSD and have some evidence to support their use (42, 248). For example, the CitAD trial showed that the addition of citalopram to a psychosocial intervention was more effective at reducing agitation and caregiver distress in people with dementia than the addition of placebo (122). Furthermore, treatment of BPSD with atypical antipsychotics has been found to cause a small yet significant reduction in caregiver burden (249). However, antipsychotics are known to increase the risk of stroke and mortality in people with dementia (112), and a recent study has found that for every 26 people with dementia treated with haloperidol, there was one death (109). Additionally, the DIADS-2 trial found that sertraline was not efficacious for the treatment of depression in people with dementia and was associated with an increased risk of adverse events (250, 251). Guidelines generally recommend that non-pharmacological treatments should be used as first line treatment of BPSD, and only when these fail should psychotropic agents be trialled for short-term use (83). Despite this, the usage of antipsychotics and other psychotropics in this vulnerable patient group remains unacceptably high (81).

Polypharmacy, which is defined as the use of five or more medications (252), is common in older people and is associated with poorer health outcomes (253). Similarly, psychotropic polypharmacy (concurrent use of two or more psychotropic agents) increases the risk of adverse events (254). Delirium super-imposed on dementia is often drug-related and medications such as opioids and benzodiazepines can trigger a delirium episode in susceptible people (255). Also, anticholinergic medications can negatively affect cognitive and physical function in older people and their use should be minimised in people with dementia (256).

Hospitalisation in people with dementia is associated with significantly poorer health outcomes (257). People with dementia are particularly vulnerable in this setting, due to the challenges of illness, new medications, and unfamiliar environments/carers (258). The INAD report of dementia care in acute hospitals found high levels of antipsychotic prescribing in hospitalised people with dementia, particularly when admitted from nursing homes (105). The authors highlighted a need for regular medication review on admission, echoed in the recently published Irish National Dementia Strategy (133). However, only 20 healthcare records from each hospital were reviewed for antipsychotic prescribing in this audit (105). Furthermore, only people with an explicit diagnosis of dementia who had a minimum length of stay of five days were included. Therefore it is unclear whether this data is representative of the majority of Irish people with dementia who are admitted to hospital.

The objectives of this study were to describe the use of psychotropic, anticholinergic and deliriogenic medication among older hospitalised patients, with and without dementia, and to identify the prevalence of polypharmacy (≥5 medications) and

psychotropic polypharmacy (concurrent use of ≥2 psychotropic agents) in these patient groups. Furthermore another key objective of this study was to examine antipsychotic prescribing patterns in patients admitted from nursing homes compared to patients admitted from their own homes. Our first research question was "*Are there any differences in the patterns of prescribing between older people (≥70 years) with and without dementia, upon admission to six acute hospitals in the south of Ireland, controlling for age, sex and co-morbidity?"* Our primary hypothesis was that people with dementia are significantly more likely to be prescribed psychotropics and to be exposed to psychotropic polypharmacy than people without dementia, as previously reported (259, 260). Our secondary hypothesis was that people with dementia are more likely to be prescribed deliriogenic and anticholinergic medications and to be prescribed more medications than people without dementia, however the evidence for this is mixed or lacking (261, 262). Our second research question was *"Are there any differences in the prevalence of antipsychotic prescribing between older people admitted to hospital from a nursing home setting compared to those admitted from their own home, controlling for age, sex, co-morbidity and dementia status?"* Our hypothesis was that older people admitted from a nursing home setting would be more likely to be prescribed an antipsychotic (104).

3.4 Methods

3.4.1 Study Design, Setting and Patients

The Cork Dementia Study has been described in detail elsewhere (100). In brief, this longitudinal observational study explored the prevalence and associations of dementia in older patients admitted to all six acute hospitals in County Cork, Ireland. County Cork has a population of 519,032 which is comprised of 49.61% males, an older population (≥70 years) of 42,382 (8.17%) (263) and an estimated dementia population of 4,830 (0.93%) (247). This is relatively comparable to the proportions for the Republic of Ireland as a whole [total population = 4,588,252; males = 49.53%; older population ≥70 years = 361,755 (7.89%) and estimated dementia population = 41,720 (0.91%)].

Eligibility criteria for this study included age ≥70 years old and elective or emergency admission (non-day case). The cut-off age of 70 years as opposed to 65 years, was decided by the original study developers (of which I was not a part of) in order to increase the 'yield' of dementia patients as the prevalence increases with age - hence maximising study efficiency (100). Recruitment occurred in each hospital for a period of two weeks and lasted from May 2012 to February 2013. Written informed consent was obtained for all patients. Exclusion criteria included patient refusal or being moribund on arrival to hospital. Patients were diagnosed with dementia by a three step approach, involving initial cognitive screening utilising the Standardised Mini-Mental State Examination (SMMSE), followed by informant-derived data utilising the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Finally,

dementia status was established by the senior author (ST), a consultant geriatrician, based on all available information (i.e. cognitive testing, informant-derived data, medical and demographic history). Patients were also assessed for delirium, depression, medication use, co-morbidity, functional ability and nutritional status. Data were prospectively collected by researchers with nursing or psychology backgrounds, after extensive training in all assessment tools. The primary researcher of this study (KW) was not involved in the initial data collection phase.

This present study is a retrospective cross-sectional analysis of the original Cork Dementia Study medication data, collected on admission. Firstly, the original medication data were cleaned by the primary researcher, a pharmacist, using a three-step cycle of screening, diagnosing and editing suspected data irregularities, for the purpose of ensuring that incorrectly-spelled or partially-filled entries could be corrected and coded accurately (264). Secondly, we coded the cleaned medication data by World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) classifications (265), excluding emollients or nutritional supplements without any active ingredients. Information on strength, quantity, duration, or usage at follow-up, were not recorded consistently so were not coded. Patients with missing medication data were excluded from the analysis. Finally, the coded medication data were cleaned again and linked at individual patient-level to the previously coded clinical data.

The *'Strengthening The Reporting of OBservational studies in Epidemiology'* (STROBE) guidelines have been followed in the conduct and reporting of this research (266).

Ethical approval was obtained from the local ethics committee (reference ECM 4 (t) 06/12/11 & ECM 3 (yy) 07/07/15) (Appendix 12)

3.4.2 Prescribing Patterns

The primary outcome in this study was the difference in prescribing patterns between people with and without dementia, focusing on psychotropic agents in people with dementia, in particular antipsychotics. The definition of a psychotropic varies significantly throughout the literature; by consensus, we included antipsychotics (N05A), antidepressants (N06A), anxiolytics (N05B), hypnotics (N05C), anticonvulsants/mood-stabilisers (N03A) and anti-dementia drugs (N06D), as these medication classes are used to manage BPSD (42). It is important to acknowledge that anti-dementia drugs are inevitably utilised more in people with dementia than people without dementia, due to their cognitive enhancing properties. Additionally, some studies do not consider anticonvulsants/mood-stabilisers to be psychotropics (267, 268). Therefore we conducted sensitivity analyses to assess the impact of more conservative psychotropic definitions on our outcomes by excluding the following in a step-wise manner:

(a) N06D (Anti-dementia drugs),

(b) N06D and N03A (Anti-dementia drugs and anticonvulsants/mood-stabilisers).

We utilised ATC codes, but reclassified Lithium (N05AN01) as a mood-stabiliser rather than an antipsychotic (269). We were also interested in psychotropic polypharmacy, and patterns of antipsychotic prescribing in those admitted from nursing homes. Other prescribing patterns of interest included the 14 main ATC anatomical groups

(excluding *'D - Dermatologicals'*), levels of minor or major polypharmacy (5-9 medications; or ≥10 medications respectively), deliriogenic medications and anticholinergics. Deliriogenic medication definition was based on published literature, decided upon by consensus between the study pharmacist (KAW) and two consultant geriatricians (ST, NOR) who are delirium experts. The included deliriogenic medications were predominantly in line with findings from a systematic review conducted by Clegg *et al.* which investigated the associations between medications and risk of delirium (255). These definitions and the associated ATC codes are shown in **Table 4**.

Table 4: Drug Class Definitions by WHO-ATC Code

Drug Class	WHO-ATC CODE
Psychotropic	
Antipsychotic	N05A (except N05AN01 - Lithium)
Antidepressant	N06A
Anxiolytic	N05B
Hypnotics	N05C
Anticonvulsants/mood stabilisers	N03A (including N05AN01 - Lithium)
Anti-dementia drugs	N06D
Potentially Deliriogenic Drugs as decided *a priori* by consensus	
Benzodiazepines	N05BA, N05CD, N03AE01
Opioids	N02A, N01AH, N02BE51, R05DA, R05FA
Dihydropyridines	C08CA
Tricyclic Antidepressants	N06AA
Anticholinergics (excluding inhaled/topical)	A03AA, A03AB, A03B, A03CA, A03CB, A03DA, A03DB, A03E, A04AD01 G04BD01-G04BD11, N02AG, N04A, N06AA,
Steroids (excluding inhaled/topical)	H02, A14A, G01B
H_2- receptor antagonists	A02BA
Anti-Parkinson's Drugs	N04
Benzodiazepine-related drugs	N05CF
Other drugs which may increase the risk of delirium but were not included in our *a priori* deliriogenic group	
Antipsychotics	N05A (except N05AN01 - Lithium)
Non-steroidal Anti-inflammatory Drugs (NSAIDS)	M01A

Antidepressants	N06A
Anti-dementia drug	N06D
Anticonvulsant/mood stabiliser	N03A (including N05AN01 - Lithium)
Typical v Atypical Antipsychotics	
Typical Antipsychotics	N05AA, N05AB, N05AC, N05AD, N05AE, N05AF, N05AG (except N05AE04 - Zisprasidone)
Atypical Antipsychotics	N05AH, N05AL, N05AX (including N05AE04 - Zisprasidone)

WHO-ATC = World Health Organisation – Anatomical Therapeutic Chemical

3.4.3 Statistical Analysis

The original data were entered into a FileMaker Pro 11 database and subsequently exported into Excel 2011 for ATC coding and linking, before transferral into STATA software version 13 (StataCorp, College Station, TX, USA) for data analysis; statistical significance at p-value <0.05 was assumed. We utilised descriptive statistics to summarise the population. We assessed differences in prescribing patterns between those with and without dementia using the χ^2 test (Fisher's exact test if expected cell frequency was <5) for categorical variables, and Student's t-test (normally distributed) or Mann-Whitney U test (non-normally distributed) for continuous variables. To control for age, sex and co-morbidity (Cumulative Illness Rating Scale in Geriatrics) effects, these were entered as independent variables into a model for each dependent variable, utilising multivariate linear or logistic regression, for continuous or binary dependent variables respectively. Results are reported in terms of adjusted odds ratios (aOR) and their 95% CI.

3.5 Results

3.5.1 Study Population Characteristics

Of 676 patients eligible for study enrolment, 598 were recruited and had a diagnosis of dementia or no dementia assigned (**Figure 18**). In total, a quarter of patients had dementia (n = 149); 53/149 (35.5%) had a known diagnosis prior to the study, and another 16/149 (11%) had known cognitive impairment. Eighty patients (53.5%) were newly (de-novo) diagnosed with dementia in the study, 29% (n = 23) of whom had moderate or severe dementia.

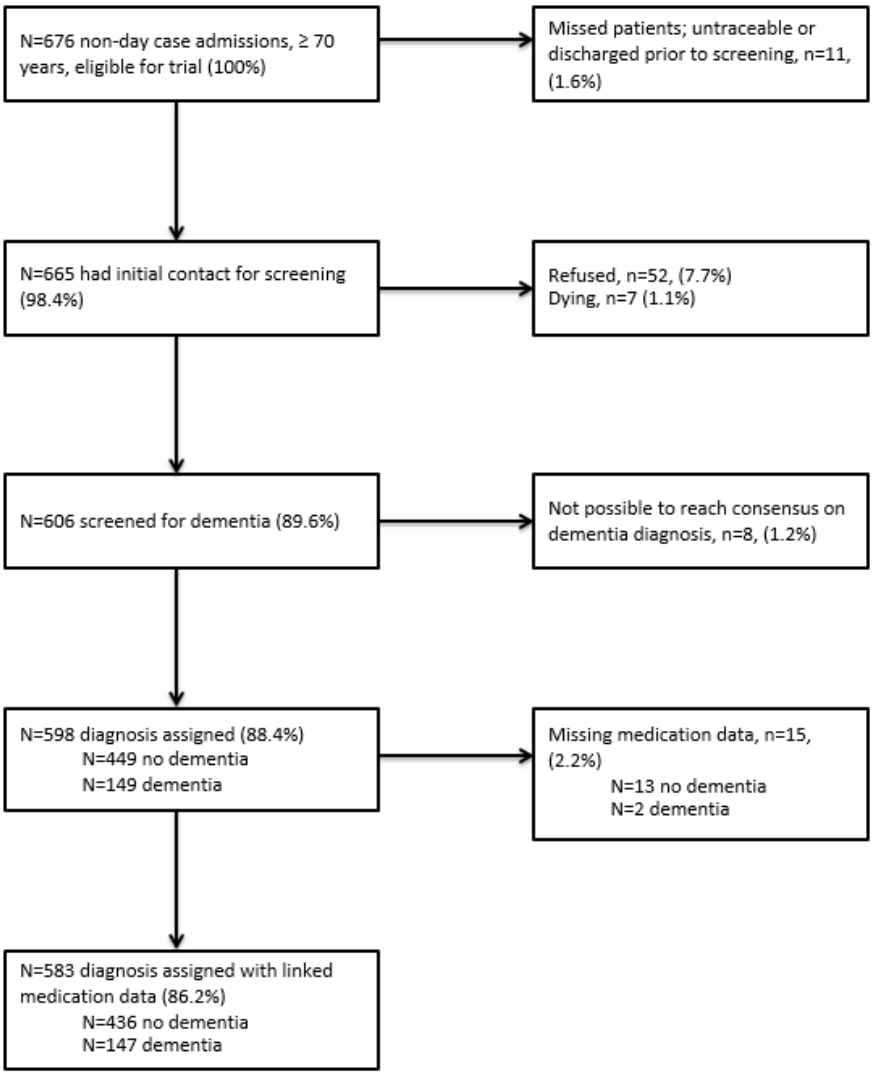


Figure 18: Flow Diagram of Participants

Fifteen patients had missing medication data, resulting in 583 patients (147 with dementia and 436 without dementia) with linked medication and clinical data. There was no significant difference in terms of the proportion of patients with missing medication data between those with and without dementia ($\chi^2 = 1.1$; p-value = 0.29). Just under half of the study population were male (49%; n = 285), the median age was 79 [IQR = 74 - 84)] and the vast majority were admitted from a home environment (own home, children's home, or social/sheltered accommodation) (91%; n = 530) (**Table 5**). People with dementia were significantly older, more

dependent and had higher co-morbidities than those without dementia (all p-values < 0.001). People with dementia were also significantly more likely to be admitted from a nursing home, to be acutely admitted to hospital, or to have delirium on admission (all p-values ≤ 0.001). One fifth (n = 115) of all patients were diagnosed with delirium at admission and people with dementia constituted the majority of these cases (73%; n = 84).

Table 5: Demographics of study population

	Dementia (n=147)[1]	No Dementia (n=436)[2]	Total (n=583)	P-value	MWU/χ^2
Sex, N (%)					
Male	63 (42.3)	222 (50.9)	285 (48.9)	0.091	χ^2=2.9
Age					
Median	84	78	79	<0.001*	MWU=-8.2
IQR	79-89	74-82	74-84		
Home Type Admitted From, N (%)					
Home	113 (76.9)	417 (95.6)	530 (90.9)	<0.001**	χ^2=56.1
Nursing Home	27 (18.4)	8 (1.8)	35 (6.0)		
Sheltered Accommodation	7 (4.8)	11 (2.5)	18 (3.1)		
CIRS-G score					
Median	11	9	10	<0.001*	MWU=-4.1
IQR	8-15	7-12	7-13		
Barthel Index					
Median	11	20	19	<0.001*	MWU=12.7
IQR	6-17	17-20	14-20		
Admission Type, N (%)					
Acute	120 (81.6)	300 (68.8)	420 (72.0)	0.003**	χ^2=9.0
Elective	27 (18.4)	136 (31.2)	163 (28.0)		
Delirium on admission, N (%)	84 (57.1)	31 (7.1)	115 (19.8)	<0.001**	χ^2=173.4

[1]N=2 dementia patients without completed medication data
[2]N=13 non-dementia patients without completed medication data
**Statistically significant at p-level <0.05, utilising MWU test.*
***Statistically significant at p-level <0.05, utilising χ2 test*
MWU = Mann-Whitney U test, CIRS-G = Cumulative Illness Rating Scale in Geriatrics, IQR = Inter-Quartile Range

3.5.2 Prescribing Patterns

Six patients were taking no medication on admission. People with dementia were prescribed almost one medication more per patient, on average, than those without dementia (mean ± SD = 7.9 ± 3.3 versus 7.1 ± 3.6; T = -2.1; p-value = 0.04) as shown in **Table 6**. However when corrected for age, sex and co-morbidity, this difference became non-significant (β = 0.3; 95% CI = -0.4 - 1.0; p-value = 0.43). The prevalence of polypharmacy was 84% in people with dementia and 77% in people without dementia, however this difference was not significant (p=0.08). Furthermore, there was no significant difference between the two groups in terms of the prevalence of major polypharmacy (27% in people with dementia and 23% in people without dementia; p-value = 0.35).

Table 6: Prescribing Patterns in Hospitalised Patients with and without Dementia

	Dementia (n=147)	No Dementia (n=436)	Total (n=583)	P-value [5]	T-value, χ^2 or Fishers exact test	Controlling for Age, Sex and co-morbidity[6]
Total number of medications prescribed	1154	3117	4271	-	-	-
Number of patients prescribed ≥ 1 medication, N (%)	147 (100)	430 (98.6)	577 (99.0)	0.15	$\chi^2 = 1.1$	aOR = 0.9, 95% CI = 0.1-4.7
Number of medications per patient						
Mean	7.9	7.1	7.3	0.04*	T = -2.1	β = 0.3, 95% CI = -0.4-1.0
SD	3.3	3.6	3.5			
Range	1-17	0-20	0-20			
Number of patients who experienced the following levels of polypharmacy, N (%):						
Minor Polypharmacy (5-9 medications)	83 (56.5)	233 (53.4)	316 (54.2)	0.53	$\chi^2 = 0.4$	aOR = 1.0, 95% CI = 0.7-1.6
Major Polypharmacy (≥ 10 medications)	40 (27.2)	102 (23.4)	142 (24.4)	0.35	$\chi^2 = 0.9$	aOR = 1.0, 95% CI = 0.6-1.6
Any Polypharmacy (≥ 5 medications)	123 (83.7)	335 (76.8)	458 (78.6)	0.08	$\chi^2 = 3.1$	aOR = 1.1, 95% CI = 0.6-1.9
Number of patients prescribed ≥ 1 of the following Psychotropic medications, N (%)						
Antipsychotics	20 (13.6)	21 (4.8)	41 (7.0)	<0.001**	$\chi^2 = 13.0$	aOR = 3.7, 95% CI = 1.8-7.6‡
Typical Antipsychotics	5 (3.4)	9 (2.1)	14 (2.4)	0.36	$\chi^2 = 0.8$	aOR = 1.6, 95% CI = 0.5-5.5
Atypical Antipsychotics	16 (10.9)	13 (3.0)	29 (5.0)	<0.001**	$\chi^2 = 14.5$	aOR = 4.7, 95% CI = 2.0-10.9‡
Antidepressants	47 (32.0)	84 (19.3)	131 (22.5)	0.001**	$\chi^2 = 10.1$	aOR = 2.1, 95% CI = 1.3-3.3‡
Anxiolytics	21 (14.3)	27 (6.2)	48 (8.2)	0.002**	$\chi^2 = 9.5$	aOR = 2.3, 95% CI = 1.2-4.6‡
Hypnotics	29 (19.7)	74 (17.0)	103 (17.7)	0.45	$\chi^2 = 0.6$	aOR = 0.9, 95% CI = 0.5-1.5
Anti-Convulsants/mood-stabiliser	16 (10.9)	50 (11.5)	66 (11.4)	0.85	$\chi^2 = 0.03$	aOR = 0.9, 95% CI = 0.5-1.7
Anti-Dementia drugs	35 (23.8)	3 (0.7)	38 (6.5)	<0.001**	F < 0.001	aOR = 47.9, 95% CI = 13.8-166.3‡
Any Psychotropic Medication[1]	99 (67.4)	182 (41.7)	281 (48.2)	<0.001**	$\chi^2 = 28.9$	aOR = 2.6, 95% CI = 1.7-4.0‡
Any Psychotropic Medication *(excluding Anti-Dementia dugs)*	83 (56.5)	182 (41.7)	265 (45.5)	0.002**	$\chi^2 = 9.6$	aOR = 1.6, 95% CI = 1.1-2.4‡

Any Psychotropic Medication *(excluding Anti-Dementia drugs and Anti-Convulsants/mood-stabilisers)*	75 (51.0)	155 (35.6)	230 (39.5)	0.001**	$\chi^2 = 11.0$	aOR = 1.7, 95% CI = 1.1-2.5‡
Number of patients who experienced the following levels of psychotropic prescribing, N (%)						
No psychotropic medication prescribed[1]	48 (32.7)	254 (58.3)	302 (51.8)	<0.001**	$\chi^2 = 28.9$	aOR = 0.4, 95% CI = 0.2-0.6‡
Only one psychotropic medication prescribed[1]	45 (30.6)	121 (27.8)	166 (28.5)	0.5	$\chi^2 = 0.4$	aOR = 1.0, 95% CI = 0.6-1.6
Psychotropic Polypharmacy[1] (≥ 2 psychotropics)	54 (36.7)	61 (14.0)	115 (19.7)	<0.001**	$\chi^2 = 35.9$	aOR = 3.5, 95% CI = 2.1-5.6‡
Psychotropic Polypharmacy (≥ 2 psychotropics) *(excluding Anti-Dementia dugs)*	43 (29.3)	60 (13.8)	103 (17.7)	<0.001**	$\chi^2 = 18.1$	aOR = 2.5, 95% CI = 1.5-4.1‡
Psychotropic Polypharmacy (≥ 2 psychotropics) *(excluding Anti-Dementia dugs and Anti-Convulsants/mood stabilisers)*	35 (23.8)	44 (10.1)	79 (13.6)	<0.001**	$\chi^2 = 17.7$	aOR = 2.7, 95% CI = 1.5-4.6‡
Number of patients prescribed ≥ 1 of the following Potentially Deliriogenic Medication[2], N (%)						
Benzodiazepines	32 (21.8)	52 (11.3)	84 (14.4)	0.003**	$\chi^2 = 8.6$	aOR = 1.7, 95% CI = 0.9-2.9
Opioids	18 (12.2)	78 (17.9)	96 (16.5)	0.11	$\chi^2 = 2.5$	aOR = 0.7, 95% CI = 0.4-1.3
Dihydropyridines	18 (12.2)	72 (16.5)	90 (15.4)	0.22	$\chi^2 = 1.5$	aOR = 0.8, 95% CI = 0.4-1.4
Tricyclic Antidepressants	9 (6.1)	17 (3.9)	26 (4.5)	0.26	$\chi^2 = 1.3$	aOR = 1.5, 95% CI = 0.6-3.6
Systemic Anticholinergics[3]	23 (15.7)	42 (9.6)	65 (11.2)	0.045**	$\chi^2 = 4.0$	aOR = 1.5, 95% CI = 0.8-2.8
Systemic steroids	7 (4.8)	40 (9.2)	47 (8.1)	0.09	$\chi^2 = 2.9$	aOR = 0.4, 95% CI = 0.1-0.9^
H_2- Receptor Antagonists	2 (1.4)	2 (0.5)	4 (0.7)	0.27	F = 0.27	aOR = 2.5, 95% CI = 0.3-23.4
Anti-Parkinson's Drugs	6 (4.1)	9 (2.1)	15 (2.6)	0.18	$\chi^2 = 1.8$	aOR = 2.0, 95% CI = 0.6-6.4
Benzodiazepine-related drugs	14 (9.5)	46 (10.6)	60 (10.3)	0.72	$\chi^2 = 0.1$	aOR = 0.7, 95% CI = 0.4-1.4
Any Potentially Deliriogenic Drug	79 (53.7)	235 (53.9)	314 (53.9)	0.97	$\chi^2 < 0.01$	aOR = 0.9, 95% CI = 0.6-1.4
Systemic NSAID[4]	5 (3.4)	29 (6.7)	34 (5.8)	0.15	$\chi^2 = 2.1$	aOR = 0.5, 95% CI = 0.2-1.5
Number of patients prescribed ≥ 1 of the following medications according to the WHO-ATC anatomical groups[7], N (%)						
Alimentary Tract and Metabolism (WHO-ATC A)	110 (74.8)	296 (67.9)	406 (69.6)	0.11	$\chi^2 = 2.5$	aOR = 0.9, 95% CI = 0.6-1.5
Blood and Blood Forming Organs (WHO-ATC B)	105 (71.4)	302 (69.3)	407 (69.8)	0.62	$\chi^2 = 0.2$	aOR = 1.0, 95% CI = 0.6-1.6
Cardiovascular System (WHO-ATC C)	126 (85.7)	381 (87.4)	507 (87.0)	0.60	$\chi^2 = 0.3$	aOR = 0.7, 95% CI = 0.4–1.3
Genito-Urinary System and Sex Hormones (WHO-ATC G)	31 (21.1)	70 (16.1)	101 (17.3)	0.16	$\chi^2 = 1.9$	aOR = 1.2, 95% CI = 0.7-2.0

Systemic Hormonal Preparations (WHO-ATC H)	25 (17.0)	100 (22.9)	125 (21.4)	0.13	$\chi^2 = 2.3$	aOR = 0.6, 95% CI = 0.4-1.0
Anti-infectives for Systemic Use (WHO-ATC J)	22 (15.0)	41 (9.4)	63 (10.8)	0.06	$\chi^2 = 3.5$	aOR = 1.6, 95% CI = 0.8-2.9
Anti-neoplastic and Immunomodulating Agents (WHO-ATC L)	5 (3.4)	26 (6.0)	31 (5.3)	0.23	$\chi^2 = 1.4$	aOR = 0.7, 95% CI = 0.2-1.9
Musculo-Skeletal System (WHO-ATC M)	38 (25.9)	100 (22.9)	138 (23.7)	0.47	$\chi^2 = 0.5$	aOR = 1.2, 95% CI = 0.8-2.0
Nervous System (WHO-ATC N)	111 (75.5)	239 (54.8)	350 (60.0)	<0.001*	$\chi^2 = 19.6$	aOR = 2.0, 95% CI = 1.3-3.2ǂ
Anti-parasitic Products, Insecticides and Repellents (WHO-ATC P)	2 (1.4)	10 (2.3)	12 (2.1)	0.74	F = 0.74	aOR = 0.6, 95% CI = 0.1-3.3
Respiratory System (WHO-ATC R)	37 (25.2)	125 (28.7)	162 (27.8)	0.41	$\chi^2 = 0.7$	aOR = 0.8, 95% CI = 0.5-1.2
Sensory Organs (WHO-ATC S)	13 (8.8)	28 (6.4)	41 (7.0)	0.32	$\chi^2 = 1.0$	aOR = 1.0, 95% CI = 0.2-2.2
Various (WHO-ATC V)	1 (0.7)	4 (0.9)	5 (0.9)	1.0	F = 1.0	aOR = 0.5, 95% CI = 0.1-5.2

*[1]Psychotropic defined as Antipsychotics, Antidepressants, Anxiolytic, Hypnotics, Anticonvulsants/mood-stabiliser and Anti-Dementia Drugs. [2]Deliriogenic Medications defined by group consensus a priori. [3]Systemic anticholinergics defined by group consensus a priori. [4]Systemic Non-steroidal anti-inflammatory drugs not included in the potentially deliriogenic drug category, but shown here for illustration purposes. [5]P-value for two-way table with measures of association [6]Adjusted Odds Ratio for dependent variable utilising linear or logistic regression as appropriate, with age, sex and CIRS-G as the independent variables. [7]WHO-ATC D (Dermatologicals) excluded as emollients without any active ingredients were not coded. *Statistically significant at p-level <0.05, utilising Student's t-test. **Statistically significant at p-level <0.05, utilising χ^2 test or Fishers exact test. ǂStatistically significant at p-level <0.05, utilising logistic regression. ^Although significant at p-level <0.05, this variable does not contain a minimum of 10 cases of event and no event that are usually required for logistic regression analysis, therefore the findings should not be interpreted as statistically significant*
CIRS-G = Cumulative Illness Rating Scale in Geriatrics, aOR = Adjusted Odds Ratio, NSAID = Non-steroid anti-inflammatory drug, WHO-ATC = World Health Organisation Anatomical Therapeutic Chemical, β = beta- coefficient, 95% CI = 95% Confidence Interval

People with dementia were significantly more likely to be prescribed at least one psychotropic medication (χ^2 = 28.9; aOR = 2.6, 95% CI = 1.7 - 4.0; p-value < 0.001). Atypical antipsychotics, antidepressants, anxiolytics and anti-dementia drugs were all significantly more likely to be prescribed to people with dementia, even controlling for age, sex and co-morbidity (all p-values < 0.05). However there was no significant difference in hypnotic, anticonvulsant/mood-stabiliser or typical antipsychotic prescription between the two groups (all p-values > 0.05). The prevalence of psychotropic polypharmacy was 37% in people with dementia and 14% in people without dementia and thus people with dementia were over three times more likely to experience psychotropic polypharmacy (χ^2 = 35.9; aOR = 3.5; 95% CI = 2.1 - 5.6; p-value < 0.001). Sensitivity analyses found that even when we excluded anti-dementia drugs and subsequently anti-convulsants/mood-stabilisers from our definition of psychotropics, people with dementia were still significantly more likely to be prescribed at least one psychotropic (p-values ≤ 0.002) and to be exposed to psychotropic polypharmacy (p-values < 0.001) than those without dementia (**Table 6**). Removing these two classes of medications reduced the prevalence of psychotropic polypharmacy in patients with and without dementia to 29% versus 14% (excluding N06D), and then to 24% versus 10% (excluding N06D and N03A) respectively.

Looking at psychotropic medications in more detail, 32% of people with dementia were prescribed antidepressants, compared to 19% of people without dementia (χ^2 = 10.1; aOR = 2.1; 95% CI = 1.3 - 3.3; p-value = 0.002). Similarly, 14% of people with dementia (n = 20) were prescribed at least one antipsychotic, compared to 5% of their peers (n = 21) (χ^2 = 13.0; aOR = 3.7; 95% CI = 1.8 - 7.6; p-value < 0.001). In terms

of those who had a previous diagnosis of dementia, 28% (15/53) were prescribed an antipsychotic, compared to just 5% (5/94) of those who had no prior diagnosis or a diagnosis of cognitive impairment. Patients admitted from nursing homes were almost five times more likely to be prescribed an antipsychotic than those who were admitted from home controlling for dementia diagnosis, age, sex and co-morbidity (χ^2 = 26.7; aOR = 4.8; 95% CI = 1.9 - 12.1; p-value = 0.001). Atypical antipsychotics (n=30) were more commonly prescribed than typical antipsychotics (n = 14), predominantly quetiapine (n = 17) and olanzapine (n = 11).

Just over half of all patients were prescribed ≥ 1 potentially deliriogenic medication (54%), with no differences in the level of prescribing of these agents between the two groups (χ^2 < 0.01; aOR = 0.9; 95% CI = 0.6 - 1.4; p-value = 0.6). Benzodiazepines and systemic anticholinergics were significantly more likely to be prescribed to people with dementia (both p-value < 0.05), but differences became non-significant after adjusting for age, sex and co-morbidity (both p-value > 0.05).

The four most commonly prescribed WHO-ATC anatomical groups were (1) cardiovascular system, (2) blood and blood forming organs, (3) alimentary tract and metabolism, and (4) nervous system, prescribed to 87%, 70%, 70% and 60% of all patients respectively **(Table 6).** There were no differences in the level of prescribing of any of the 13 included WHO-ATC anatomical groups (all p-values > 0.05), except for nervous system drugs, which were more commonly prescribed to people with dementia (χ^2 = 19.6; aOR = 2.0, 95% CI = 1.3 - 3.2; p-value = 0.003).

3.6 Discussion

3.6.1 Main Findings

This retrospective cross-sectional study aimed to explore the prescribing patterns of psychotropic, anticholinergic and deliriogenic medications, and polypharmacy, in a well-defined cohort of hospitalised older Irish patients; and to assess differences between people with and without dementia. Overall, we found that this population was prescribed high levels of medication, with over three-quarters experiencing polypharmacy and a quarter experiencing major polypharmacy. People with dementia were more likely to be prescribed psychotropic medications and to experience psychotropic polypharmacy. We found no differences in the prescribing patterns in terms of number of medications, anticholinergic medications, deliriogenic medications or any of the other main WHO-ATC anatomical groups, except for nervous system medications.

Another important finding of the Cork Dementia Study was that only 35.5% of people with dementia had an explicit diagnosis of dementia prior to the study. Previous studies conducted in Australia (270) and the UK (271) reported similar levels of under-diagnosis in people with dementia requiring an admission to hospital. This low rate of diagnosis may result in inappropriate medications being prescribed to people with dementia and hospital physicians incorrectly assuming capacity to consent for complex treatments (100).

Our results are in agreement with several pharmacoepidemiological studies, which found a high prevalence of psychotropic medicine use in older hospitalised patients

in general (272), and significantly higher levels of psychotropic medications being prescribed to people with dementia than to those without dementia (259, 273-275). These findings are not surprising due to the ubiquity of BPSD in dementia. One large scale study of the longitudinal course of BPSD in people with dementia reported a five-year period prevalence of BPSD symptoms of 97% (36). The most commonly reported symptoms were apathy, depression and delusions. Of note in this study, many people with dementia already had BPSD at the time of initial dementia diagnosis. Furthermore, many studies have reported the presence of BPSD in Mild Cognitive Impairment (MCI) (276). There are very recently published criteria for diagnosing Mild Behavioural Impairment (MBI) (277) that describe BPSD as a possible index manifestation of dementia, in advance of measurable cognitive impairment. This is an important conceptual advance in our understanding of dementia, and the prescription of psychotropic medications for changes in behaviour or personality may give an indication of an emergent dementia. Furthermore, benzodiazepines are often associated with cognitive decline and dementia (278); with the implication of causality between the two, although a recent study has questioned this causal association (279). An alternative hypothesis is that anxiety can present as the index manifestation of dementia, with benzodiazepines prescribed, and when the underlying dementia ultimately declares itself, the benzodiazepine is labelled as the culprit for cognitive decline (277). The bottom line is that BPSD are fundamental and core features of dementia, and result in greater illness burden, higher caregiver burden, poorer quality of life, higher rates of institutionalisation, faster cognitive decline and death, and are associated with greater plaque and tangle burden (36, 280, 281).

Notwithstanding these important contextual issues, the fact remains that people with dementia are often excessively and inappropriately prescribed psychotropic medications, and for prolonged periods of time (128). We know that in people with dementia, antipsychotics significantly increase the risk of stroke and mortality (109) and benzodiazepines significantly increase the risk of falls and hip fractures (282). Prescription of multiple psychotropic agents results in even greater risk of adverse events (254). It is imperative that prescribers and care providers adhere to guidelines, in so far as possible, by utilising non-pharmacological interventions in the first instance and prescribing antipsychotics as a last resort, with regular review and trials of withdrawal (83). There is evidence to support the use of non-pharmacological interventions in managing BPSD (283), however better quality trials are required in this area.

The prevalence of antipsychotic usage in the pharmacoepidemiological studies mentioned above ranged from 5% to 43% in those with dementia, highest in studies looking at institutionalised patients. In comparison, the prevalence of antipsychotic usage in people with dementia in our study, where 91% of patients were admitted from a home environment (and hence predominantly reflecting primary care prescribing patterns) was 14%, lower than a previous study of home-dwelling older people (33%) (259). This probably reflects the high rate of undiagnosed cases in our study, with only 35.5% having a prior diagnosis. The rates of prescribing in our study population with known dementia was 28%, similar to that found in the study by Hartikainen *et al*. The INAD study conducted in 2013 found that 41% of people with dementia were prescribed antipsychotic medications during their admission in Irish hospitals, and also found poor levels of documentation of mental health assessment

and drug indication (104, 105). This figure is much higher than what we found in our study, and may reflect the purposeful selection of patients for the audit who had an explicit diagnosis of dementia and a longer length of stay, thereby potentially representing a much frailer sub-population of people with dementia. Additionally, as the data were collected on admission to hospital, the prescribing patterns captured in our study, better reflects primary care prescribing practices rather than in-patient prescribing practices. Nonetheless, the high figure reported in the INAD study is still alarming, considering the same audit conducted in England and Wales in 2012-2013 (130) and Northern Ireland in 2014-2015 (284) found much lower levels of antipsychotic prescribing; 18% and 21% respectively.

We found that patients admitted from a nursing home (n=35) were almost five times more likely to be prescribed an antipsychotic than those admitted from other home types. The INAD report also found that people with dementia admitted from nursing homes were significantly more likely to be prescribed an antipsychotic compared to those admitted from their own home (46% v 19%; $p < 0.001$) (104, 105). Similarly, a cross-sectional Finnish nursing home population study found that 43% of residents were prescribed antipsychotics (275). These findings would indicate that in a busy hospital setting, pharmacists and other healthcare professionals should prioritise people with dementia, along with patients admitted from nursing homes, for review of their antipsychotic medications. However, as discussed in Chapter 2, there is a distinct lack of such studies conducted in hospitalised dementia patients. It is important that any antipsychotic medication review conducted in a hospital setting involves effective communication with the patient's General Practitioner (GP), carers and nursing home staff, as it is necessary to know the indication for the antipsychotic

and whether any non-pharmacological intervention or dose reduction had been previously attempted (285). It is also crucial that these community-based care providers are informed of any plans for dose titrations or withdrawals at hospital discharge to prevent the unintended re-commencement of these patients on antipsychotics. Additionally, as the highest prevalence of antipsychotic prescribing occurred in those admitted from nursing homes, future interventions aimed at improving the appropriateness of antipsychotic prescribing in people with dementia may be more worthwhile if conducted in nursing home as opposed to acute settings.

We did not find any significant differences in terms of anticholinergic, deliriogenic or total number of medications prescribed between the two patient groups. We were surprised by the former finding, as previous studies have reported higher levels of anticholinergic prescribing in people with dementia (286). One potential hypothesis is that a greater level of awareness surrounding the risk of cognitive decline with these agents has resulted in more careful prescribing in people with dementia. However a repeated cross-sectional study conducted in Scotland found that despite the increasing evidence surrounding the adverse effects of anticholinergics, exposure to these agents in older adults has actually increased in recent years (287). We were unable to find literature on the prevalence of deliriogenic medication usage in people with dementia, thus our *a priori* hypothesis on this topic was purely speculative, based on the knowledge that the people with dementia in the study had more co-morbidities than their peers. Further research should be conducted to investigate the consequences of deliriogenic prescribing in people with dementia. The evidence on medication burden in people with dementia is mixed, with some studies finding people with dementia are prescribed more (261) and others finding they are

prescribed less medications (262) than people without dementia. The discrepancies may relate to population differences between the studies.

3.6.2 Strengths and Limitations

The main strength of this research was the large number of patients recruited into this multi-centred trial and the vast amount of rich data that were collected from each patient allowing us to tease apart effects of dementia from confounding factors such as age, sex and co-morbidity. However, when the sample size for the primary outcome (i.e. the difference in proportion of patients with and without dementia who were prescribed at least one psychotropic – based on the most conservative definition for a psychotropic) was retrospectively calculated, it was clear that this study was not powered to detect this difference. In terms of comparing two proportions using α=0.05 and power of 80%, it was calculated that 159 patients would be required in each group to detect a statistically significant difference between 51% and 35.6%. Although 436 patients without dementia were recruited into this study, only 147 patients with dementia were recruited. Hence caution should be used when interpreting these findings.

The main limitation of this study is the retrospective nature of the medication analysis, so that it was not possible to resolve any ambiguous medication data entries. However the quality of data collection was quite high and this ambiguity rarely occurred. Secondly, as the study is observational, it is not possible to draw any conclusions on causality, as dementia or cognitive impairment may have been the cause of or potentially even the result of differences in medication usage between the two patient groups. Thirdly, the lack of information on strength, quantity and

duration of medication usage is a limitation to our study. It would have been interesting to investigate the differences in dosing within and between the two patient groups, as toxicity with antipsychotics, for example, is largely dose-dependent (288). Finally, as the study was conducted in only one county in Ireland, the findings may not be representative of the entire older Irish population. However, as the demographic profile of Cork County is relatively similar to that of the rest of the country, we believe these results may possibly be representative of the entire older Irish population.

3.7 Conclusion

Psychotropic drug use and polypharmacy is highly prevalent, and dementia is under-diagnosed among older Irish hospitalised patients. People with dementia are more likely to be prescribed antipsychotics, antidepressants, anxiolytics and anti-dementia drugs. People with dementia are also more likely to be exposed to psychotropic polypharmacy. These differences in prescribing patterns may be largely attributed to BPSD in dementia, and neuropsychiatric symptoms in pre-dementia clinical syndromes like MCI and MBI. Longitudinal research is required to assess the long-term impact that medication usage or non-usage has on the development of dementia in older people and also to assess the impact that a diagnosis of dementia has on the physician's prescribing patterns. Furthermore, as the highest prevalence of antipsychotic prescribing occurred in those admitted from nursing homes, future interventions aimed at improving the appropriateness of antipsychotic prescribing in

people with dementia may be more worthwhile if conducted in nursing home as opposed to acute settings.

Chapter 4. Influences on Decision-Making Regarding Antipsychotic Prescribing in Nursing Home Residents with Dementia: a Systematic Review and Synthesis of Qualitative Evidence

4.1 Chapter Description

In Chapter 3, I established that psychotropic drug use is highly prevalent in older Irish adults on admission to hospital, especially in those with dementia. From examination of the patterns of prescribing in this study, it was evident that antipsychotic prescribing was most prevalent in those admitted from nursing homes. Hence, in order to effectively target inappropriate antipsychotic prescribing to people with dementia in a future intervention, I realised that the best option would be to focus on nursing home settings. In this chapter, I conduct a meta-ethnography, essentially exploring the reasons why antipsychotics continue to be inappropriately prescribed to nursing home residents with dementia. Collating and understanding what is known on this complex topic, are important first steps in the development of an evidence-based, theory-informed intervention. An addendum is provided at the end of this chapter with a discussion of up-to-date search results.

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4.2 Abstract

4.2.1 Background

Antipsychotic prescribing is prevalent in nursing homes for the management of BPSD, despite the known risks and limited effectiveness. Many studies have attempted to understand this continuing phenomenon, utilising qualitative research methods, and have generated varied and sometimes conflicting findings. To date, the totality of this qualitative evidence has not been systematically collated and synthesised.

4.2.2 Aims

To synthesise the findings from individual qualitative studies on decision-making and prescribing behaviours for antipsychotics in nursing home residents with dementia, with a view to informing intervention development and quality improvement in this field.

4.2.3 Methods

A systematic review and synthesis of qualitative evidence was conducted (PROSPERO protocol registration CRD42015029141). Six electronic databases were searched systematically from inception through July 2016 and supplemented by citation, reference and grey literature searching. Studies were included if they utilised qualitative methods for both data collection and analysis, and explored antipsychotic prescribing in nursing homes for the purpose of managing BPSD. The Critical Appraisal Skills Programme (CASP) assessment tool was utilised for quality appraisal. A meta-ethnography was conducted to synthesise included studies. The Confidence

in the Evidence from Reviews of Qualitative research (CERQual) approach was used to assess the confidence in individual review findings. All stages were conducted by at least two independent reviewers.

4.2.4 Results

Of 1,534 unique records identified, 18 met the inclusion criteria. Five key concepts emerged as influencing decision-making: *Organisational Capacity; Individual Professional Capability; Communication and Collaboration; Attitudes; Regulations and Guidelines*. A *'line of argument'* was synthesised and a conceptual model constructed, comparing this decision-making process to a dysfunctional negative feedback loop. Our synthesis indicates that when all stakeholders come together to communicate and collaborate as equal and empowered partners, this can result in a successful reduction in inappropriate antipsychotic prescribing.

4.2.5 Conclusion

Antipsychotic prescribing in nursing home residents with dementia occurs in a complex environment involving the interplay of various stakeholders, the nursing home organisation and external influences. In order to improve the quality of antipsychotic prescribing in this cohort, a more holistic approach to BPSD management is required. While we have found the issue of antipsychotic prescribing has been extensively explored using qualitative methods, there remains a need for research focusing on how best to change the prescribing behaviours identified.

4.3 Introduction

Antipsychotics are commonly prescribed to manage BPSD (128). These medications have a role to play in BPSD when there is a danger of harm to self or others, when there is a psychosis, or when non-pharmacological approaches have not been effective (289). However, these agents are often prescribed inappropriately, despite evidence of an increased risk of stroke and mortality, and a lack of effectiveness in these patients (109, 112, 128). As discussed in Chapter 3, people with dementia are prescribed significantly more of these agents than the general older population (2, 290) and it is in the nursing home setting where the majority of this prescribing occurs (291).

A 2014 systematic review found that many interventions are effective in the short-term at reducing the inappropriate prescribing of antipsychotics in nursing homes to people with dementia (151). The authors highlighted the need for a greater understanding of the contextual drivers of inappropriate prescribing in order to improve the long-term sustainability of the reviewed interventions.

Qualitative research allows for a rich understanding of complex social environments such as nursing homes and can be used to develop and improve interventions in this context (292). A number of original qualitative studies have been conducted on antipsychotic prescribing in people with dementia but to date these have not been the subject of a systematic review.

The most commonly utilised method for synthesising qualitative evidence is meta-ethnography (293). This seven-step method of qualitative evidence synthesis

employs an inductive approach moving from specific observations to broader generalisations. It is a systematic interpretive approach that is particularly useful for generating new theories or concepts, which can influence policy and practice (294). For example, recently published clinical guidelines on multimorbidity (295) have been informed by a high-quality meta-ethnography in this similarly complex field (296).

The aim of our study was to synthesise the findings from individual qualitative studies in order to develop novel interpretations of the influences on decision-making regarding the prescribing of antipsychotics in nursing home residents with dementia, with a view to informing intervention development and quality improvement in this field.

4.4 Methods

We conducted a systematic search of primary qualitative studies exploring antipsychotic prescribing in non-acute, long-term care institutions. We used a *'meta-ethnographic synthesis'* (293), as adapted by Atkins *et al*. (297) to guide our methods. The review protocol was registered with the PROSPERO international prospective register of systematic reviews (registration number: CRD42015029141) (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=29141).

Six electronic databases were searched from inception to July 2016; Medline, PubMed, EMBASE, CINAHL, PsycINFO and Academic Search Complete. Database-specific search strategies were developed with assistance from a medical librarian. Search terms included a combination of Medical Subject Heading terms, keywords

and a comprehensive list of synonyms of the following: 'dementia' AND 'prescription' AND 'antipsychotic agents' with the aim of being as sensitive as possible. Qualitative-specific search terms such as 'interview' and 'qualitative' were not used, as we believed this may have hindered discovery of poorly labelled, yet potentially relevant, mixed-methods studies. The search was not limited by dates of publication or country of origin. To supplement the database search, we conducted hand-searches of key journals and conference proceedings; citation searches of highly cited key studies; reviews of reference lists of key studies; and contacted authors of relevant conference abstracts and studies. The grey literature search was further supplemented by checking the first 100 hits from Google Scholar and by consulting the websites and key personnel from various international Alzheimer's Societies (Appendix 2). Google Scholar has been found to be a useful method for locating relevant qualitative studies with high yields, in a previous meta-ethnography (298).

We included any English-language, peer-reviewed primary study, published in full, using recognised qualitative research methods of both data collection (e.g. focus groups, semi-structured interviews, ethnographic approaches and documents) and analysis (e.g. grounded theory, narrative analysis, thematic analysis, framework analysis, discourse analysis and interpretive phenomenological analysis). Mixed-methods studies were only included if they utilised qualitative methods as a component of the study. Only the qualitative components of these studies were extracted for analysis. We only included questionnaire studies if the written comments had been analysed using qualitative methods. Studies which did not provide an account of the qualitative methods of data collection or data analysis were excluded, even if the study referred to itself as a qualitative study.

Through our initial scoping of the literature, it became clear that the terms *'antipsychotic', 'psychotropic', 'psychoactive'* and *'pharmacological interventions'* are often used interchangeably, especially in terms of managing BPSD. Some studies included nursing homes and community settings, making it difficult to disentangle nursing home specific findings. Furthermore, not all studies explicitly stated that the nursing home residents had dementia, even though evidence shows the vast majority of nursing home residents have dementia. To avoid missing potentially relevant findings, we made a decision to include studies (otherwise meeting our inclusion criteria) that explored the prescription of *'pharmacological agents'* (with at least implied inclusion of antipsychotics) for the purpose of managing BPSD in people with dementia (in any setting where there is at least some explicit mention of nursing homes). Studies exploring management of other mental health conditions (e.g. schizophrenia), other specific settings (e.g. acute hospital) where there is no explicit reference to nursing homes, or those explicitly referring to other specific psychotropic agents (e.g. antidepressants) were considered to be beyond the scope of this review and were excluded.

For the first stage of study selection, one reviewer (KW) conducted preliminary screening of titles to exclude records that were clearly not relevant (e.g. pre-clinical studies). For the second stage, two reviewers (KW and RD) independently screened titles and abstracts, against inclusion criteria, to identify potentially relevant studies. In the third stage, two reviewers (KW and RD) independently reviewed full texts of studies. Consensus on inclusion in stages two and three was reached by discussion between both reviewers, with arbitration by a senior reviewer (ST) if required. The CASP assessment tool for qualitative research was used to assess the quality of

included studies (299), by two reviewers (KW and JB) independently, and consensus was reached by discussion. Studies were not excluded based on the assessed level of quality. Methodological limitations of included studies were accounted for in the CERQual assessments (discussed below) (300).

Four reviewers (KW, RD, EC and CS) read and re-read the included studies, with a focus on the content and context. As a group, we identified what we believed to be the conceptually-richest *'index paper'* (301), and used this as the starting point. Three reviewers (KW, RD and EC) read all 18 included studies starting with the *'index paper'* and then chronologically. One reviewer (KW) open coded the study findings of all included studies (results and discussion sections), focusing specifically on first-order interpretations (views of the participants) and second-order interpretations (views of the authors). To ensure credibility and dependability of coding, another reviewer (CS) coded the *'index paper'* and two other randomly selected studies (91, 302), and differences in interpretation were discussed and consensus reached (303). The four reviewers convened several times to discuss independently derived concepts and patterns from the studies. Reflexivity was preserved as one reviewer (KW) conducted memo writing (303). As a multidisciplinary group, we were cognisant of our professional biases, therefore we ensured that there was a balance between clinical (KW and CS) and non-clinical (EC and RD) reviewers at this stage.

Collectively, we developed five key concepts to reflect the main findings of all included studies. We developed a matrix of these concepts and assessed how each individual study related to each concept (Appendix 4) Two reviewers (KW and SB) independently extracted data regarding contextual information from each included

study. Discrepancies were resolved through discussion between both reviewers. QSR International's NVivo version 11 was used to assist with data analysis and synthesis (304).

In line with the constant comparative method of qualitative analysis (305), the first- and second-order interpretations were compared and contrasted across primary studies to identify similarities and disagreements. The importance of context to each interpretation was carefully observed. In this way, reciprocal (when concepts in one study can incorporate those of another) and refutational translations (when the concepts in different studies contradict one another) were conducted (294). All eight reviewers were involved in this and the following stages to ensure no important meanings were lost upon translating one study into the next.

We collaboratively developed third-order interpretations by synthesising first- and second-order interpretations, from each study. The synthesis required refining the key concepts and building on the analysis iteratively. This process was repeated until we were satisfied that the third order interpretations added to, but were still representative of, the findings of the total dataset. These interpretations act as testable, novel hypotheses, which are still grounded in the data (297). We then linked these using a *'line of argument'* in order to develop an overarching conceptual model explaining the phenomenon (296). Noblit and Hare describe this *'line of argument'* synthesis as a means of uncovering novel understandings that were hidden in the individual studies (discovering a *'whole'* among a set of parts) (293).

We reported our results in line with the *'ENhancing Transparency in REporting the synthesis of Qualitative research'* (ENTREQ) statement (306) (Appendix 3) and

expressed our search strategy results as a PRISMA flow diagram (197) (**Figure 19**). To present the findings of the review in a manner useful for policy-makers, we used CERQual (300). This tool allows assessment of the confidence in synthesised qualitative findings. We assessed the extent to which the review findings (i.e. third-order interpretations) were reasonable representations of the phenomenon of interest, by independent application of CERQual, by two reviewers (KW and RD), with discussion until consensus was reached.

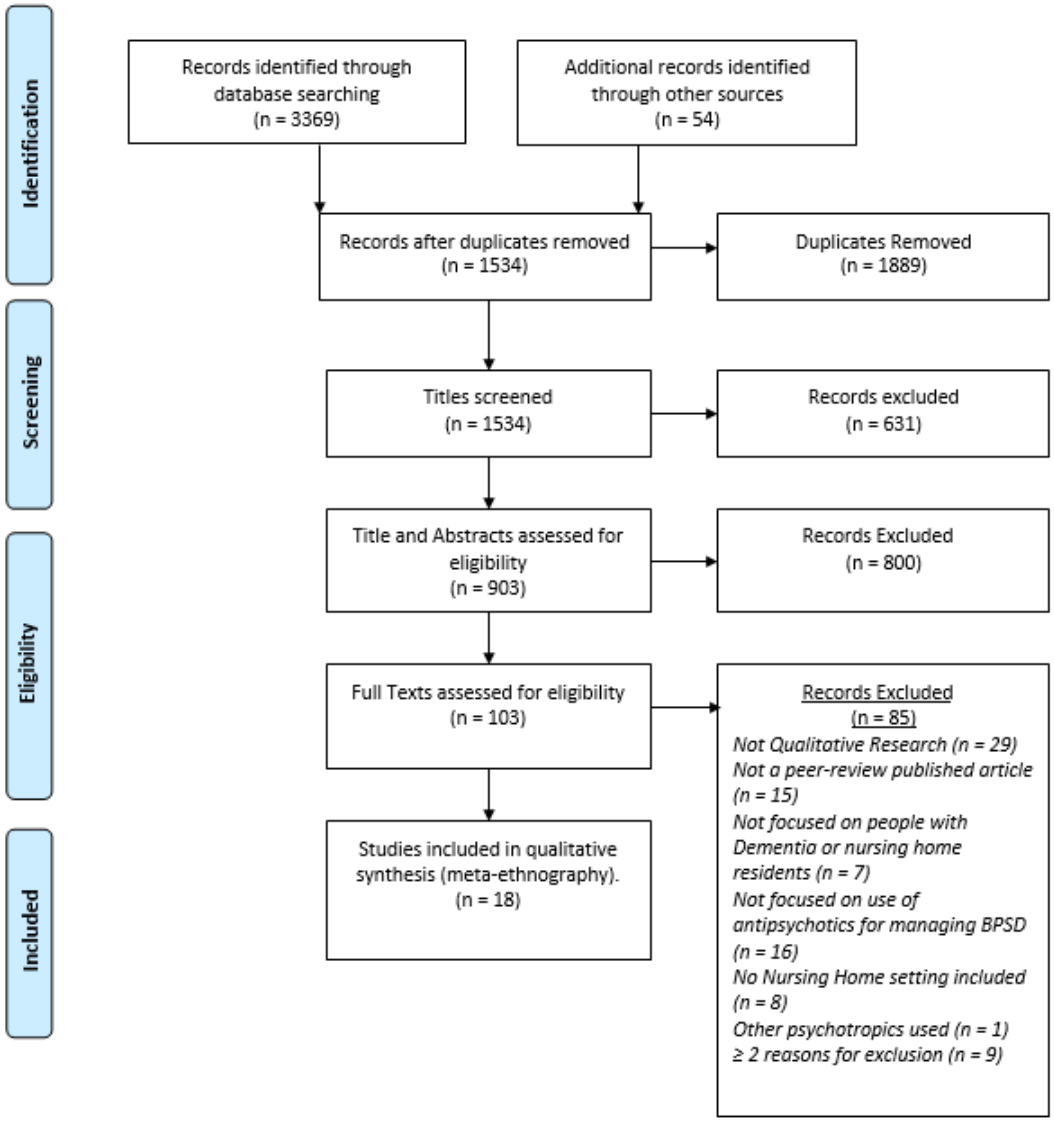

Figure 19: PRISMA flow diagram of search strategy results.

4.5 Results

4.5.1 Search Results

A total of 1,534 unique records were found after duplicate removal (**Figure 19**) (197). After the exclusion of records based on title screening (n=631) and subsequent title and abstract screening (n=800), the remaining 103 full texts were assessed for eligibility. We excluded 85 records at this stage. In our final review, we included 18 studies describing 17 study cohorts.

4.5.2 Characteristics of Included Studies

Table 7 outlines the characteristics of the 18 included studies. The studies were conducted in six different countries: UK (n =7) (64, 91, 307-311), US (n =5) (302, 312-315), Australia (n = 3) (90, 316, 317), Canada (n = 1) (58), The Netherlands (n = 1) (301) and South Africa (n = 1) (318). Eleven of the studies employed a purely qualitative methodology, (64, 90, 91, 301, 302, 307, 308, 311, 316-318) while seven utilised mixed-methods (58, 309, 310, 312-315). A total of 1,609 unique participants were involved: nurses (n=479), other nursing home staff (n=657), family carers (n=239), physicians (n=144), pharmacists (n=49) and old age advocates (n=6). One study did not provide a disciplinary breakdown for its 35 participants (302). No study included the voice of the person with dementia. Of the 114 included nursing homes that had their 'for-profit' status described, 68 were for-profit, 40 were not-for-profit and 6 were described as "other".

Table 7: Characteristics of Included Studies

First Author	Year of Publication	Country	Study Objectives	Methods	Data Collection	Qualitative Data Analysis	Participant characteristics (n)	Setting (n)
Foley (312)	2003	US	To explore staff perceptions of successful management of severe behavioural problems in dementia SCUs	M	Structured interviews with some open ended questions	Content analysis	Nursing staff (19), Activities co-ordinator or Social Worker* (4), unit co-ordinators [Nurses or Social Workers]* (9), Unknown Staff Role (4). Total participants (36)	Nursing Home SCUs (36)
Patterson (307)	2007	UK	To assess the suitability of an American model of pharmaceutical care for nursing home residents for application in nursing homes in the UK	Q	Focus groups and semi-structured interviews	Framework	Clinical Pharmacists (6), Resident Advocates (6), Prescribing Support Pharmacists (14), GPs (8), Nursing Home Managers (10). Total participants (44)	Participants worked in in-patient, GP, nursing home and charity organisations settings (unknown numbers) §
Wood-Mitchell (64)	2008	UK	To examine the process by which consultant old age psychiatrists prescribe for BPSD and explore the factors that influence their decision	Q	Semi-structured interviews	Grounded theory	Consultant Old Age Psychiatrists (8). Total participants (8)	Psychiatrists worked in in-patient and community-care settings (unknown numbers) §
Kolanowski (302)	2010	US	To explore nursing, recreational therapy and medical staff perceptions of barriers to the implementation of non-pharmacological interventions for BPSD	Q	Focus groups	Content and thematic	Registered Nurses, Licensed Practical Nurses, Certified Nursing Assistants, Recreational Therapists, Activity Personnel and Medical Directors. Total participants (35)†	Nursing Homes (6)
Molinari (314)	2011	US	To explore the justification of psychoactive medication prescription for new nursing home residents	M	Chart review with follow up focus groups	Content and thematic	Licensed Practical Nurses (8), Certified Nursing Assistants (20), Registered Nurses (13), Medical Directors (1), Social Workers (2). Total participants (44)	Nursing Homes (7)
Duxbury (308)	2013	UK	To explore the views of nurses, and relatives regarding the causes of, and most effective ways of responding to aggressive behaviour from people with dementia in residential care settings	Q	Semi-structured interviews with staff. Focus Groups with relatives	Thematic	Dementia Care Unit Manager (4), Registered Nurses (2), Care Assistants (2), Relatives (8). Total participants (16)	Nursing Homes (4)
Harding (309)	2013	UK	To explore carers experiences of the use of antipsychotic medications in people with dementia	M	Surveys with open ended questions (online and paper), focus groups and in-depth interviews	Inductive and deductive coding. Thematic	Carers and former carers of people with dementia (190). Total participants (190)	Mixture of own home, nursing home and residential home (unknown numbers) §
Janzen (58)	2013	Canada	To investigate the perceptions of LTC staff regarding the current use of NPI for reducing agitation in seniors with	M	Focus groups, semi-structured interviews and a survey with some	Hermeneutic phenomenology	Registered Nurses (8), Registered Practical Nurses (13), Personal Support Workers (8), Recreation Specialist or Coordinators (6), Directors of Care (3), Unit Coordinators (2), Recreation Assistant (1), Resident	LTC facilities (5)

			dementia and to identify facilitators and barriers that guide NPI implementation		open ended questions		Assessment Instrument Coordinator (1), Dietary Specialist (1), Art Therapist (1). Total participants (44)	
Mavrodaris (310)	2013	UK	To investigate antipsychotic prescribing practices and patient review in primary care settings	M	Survey with some open ended questions.	Thematic	GPs (60), care home staff (28). Total participants (88)	GP surgeries (60) and care homes (28) §
Ervin (316)	2014	Australia	To explore residential aged care staff perceptions of the limitations to five commonly used methods of managing BPSD; pharmacological therapy and behavioural, emotional, cognitive and stimulation therapies	Q	Survey with open ended questions.	Interpretive Description	Division 1 Registered Nurse (33), Division 2 Medication Endorsed Registered Nurse (29), Division 2 Registered Nurse (34), Personal Care Assistant (14), Students or Activities Coordinator (17), Not specified (3). Total participants (130)	Residential aged care facilities (6)
Smeets (301)	2014	The Netherlands	To explore factors that elucidate reasons for psychotropic drug prescription for neuropsychiatric symptoms in nursing home residents with dementia	Q	Semi-structured interviews	Grounded theory	Elderly Care Physician (13), Resident in Elderly Care Medicine (1), Medical Doctor (1), Registered Nurses (4), Certified Nurse Assistants (9), Nurse Assistant (1). Total participants (29)	Nursing Homes (12)
Bonner (315)	2015	US	To describe the rationales that providers and family members cite for the use of Antipsychotic medications in people with dementia living in nursing homes	M	Medical Record Abstraction and Open ended interviews	Directed content analysis	Directors of Nursing (26), Registered Nurses and Licensed Practical Nurses (91), Certified Nursing Assistants (244), Physicians and Advanced Practitioner Prescribers (27), Pharmacists (23), Psychiatrists (14), Family Members (41). Total participants (466)	Nursing Homes (26)
Ellis (313)	2015	US	To explore strategies that have been implemented, to assess which strategies are evidence-based, and to make recommendations to improve upon practice to reduce antipsychotic medication use	M	Survey with both descriptive and open-ended questions.	Theme-based content analysis	Director of Nursing (109), Nursing Home Administrator (95), Social Worker (7), Other Nursing Home Staff (65). Total Participants (276)	Nursing Homes (unknown number, approximately 227)
Lawrence (311)	2015	UK	To contribute to an optimised training programme for care staff that supports the implementation of evidence-based psychosocial interventions in long-term care	Q	Focus groups	Thematic with constant comparison method	Care Assistants (53), Senior Care Assistants (30), Activity Therapists (13), Registered Nurses (6), Deputy Managers (5), Managers (2), Other Staff (10). Total participants (119)	Care Homes (16)
Sawan (90)	2016	Australia	To explore how visible artefacts in nursing homes influence the prescribing and use of psychotropic medicines, and how these artefacts were operationalised across nursing homes	Q	Semi-structured interviews	Thematic	Managers (8), Registered Nurses (8), Nursing Assistants (5), GPs (8), Pharmacists (6), Enrolled nurses (2), Specialist medical practitioner (1), Nurse Practitioner (1), Clinical Nurse Consultant (1). Total participants (40) ‡	Nursing Homes (8)

Sawan (317)	2016	Australia	To explore the key dimensions of organisational climate and their subsequent influence on the use of psychotropic medicines	Q	Semi-Structured Interviews	Thematic	Managers (8), Registered Nurses (8), Nursing Assistants (5), GPs (8), Pharmacists (6), Enrolled nurses (2), Specialist medical practitioner (1), Nurse Practitioner (1), Clinical Nurse Consultant (1). Total participants (40) ‡	Nursing Homes (8)
Shaw (91)	2016	UK	To explore and understand treatment culture in prescribing of psychoactive medications for older people with dementia in nursing homes	Q	Semi-structured interviews	Thematic and framework	Managers (5), Nurses (7), Care Assistants (13), GPs (2). Total participants (27)	Nursing homes (6)
Van Wyk (318)	2016	South Africa	To gain an understanding of what care home staff perceive to be distressed behaviour, their coping strategies and how they learned to work with residents with behavioural symptoms of dementia.	Q	Semi-structured interviews	Thematic and framework	Care Assistants (17). Total participants (17)	Care Homes (4)

Q, Qualitative Methods; M, Mixed Methods; BPSD, Behavioural and Psychological Symptoms of Dementia; NPI, Non-pharmacological interventions; LTC, Long-term care; SCU, Specialist Care Unit; GP, General Practitioner (also known as Primary Care Physicians).

** Study did not obtain specific degree affiliation, thus unable to distinguish between social workers and nursing staff. † Unknown breakdown of participants. § Research participants may not have been based in a Nursing Home Setting, but focus of study is on people with dementia in the Nursing Home Setting. ‡ The same study cohort in both studies.*

4.5.3 Quality Appraisal

The overall quality of included studies was assessed to be moderate to high for 17 of the 18 studies (**Table 8**). A common weakness, found in twelve studies, was inadequate researcher reflexivity (301, 302, 307-314, 316, 318). The relationship between the researcher and participants had not been effectively addressed in these studies. The overall quality of one study was assessed to be low due to concerns across several CASP domains (309). Despite these weaknesses, we believed that on the whole, these studies were sufficiently robust to contribute to our meta-ethnography and to the development of our conceptual model

Table 8: Quality Appraisal of Included Studies

First Author (Year of Publication)	Clear Statement	Qualitative Appropriate	Research Design	Sampling	Data Collection	Reflexivity	Ethics	Data Analysis	Discussion of Findings	Value	Overall Assessment of methodological quality
Foley (2003) (312)	√	√	√	?	?	x	?	?	√	√	Moderate
Patterson (2007) (307)	√	√	√	√	√	x	√	√	√	√	Moderate-to-High
Wood-Mitchell (2008) (64)	√	√	√	?	√	√	?	?	√	√	Moderate-to-High
Kolanowski (2010) (302)	√	√	√	?	?	x	√	√	√	√	Moderate-to-High
Molinari (2011) (314)	√	√	√	x	?	x	?	√	√	√	Moderate
Duxbury (2013) (308)	√	√	√	√	?	x	√	√	√	√	Moderate-to-High
Harding (2013) (309)	√	√	√	√	x	x	?	x	x	x	Low
Janzen (2013) (58)	√	√	√	√	√	√	√	√	√	√	High
Mavrodaris (2013) (310)	√	√	√	√	?	x	?	?	√	√	Moderate
Ervin (2014) (316)	√	√	√	√	?	x	√	√	√	√	Moderate
Smeets (2014) (301)	√	√	√	?	√	x	√	√	√	√	Moderate-to-High
Bonner (2015) (315)	√	√	√	√	√	√	√	x	√	√	Moderate
Ellis (2015) (313)	√	√	√	x	√	x	?	√	√	√	Moderate

Lawrence (2015) (311)	**√**	**√**	**√**	**√**	**√**	**x**	**√**	**√**	**√**	**√**	**Moderate-to-High**
Sawan (2016) (90)	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**High**
Sawan (2016) (317)	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**High**
Shaw (2016) (91)	**√**	**√**	**√**	**?**	**√**	**√**	**√**	**√**	**√**	**√**	**High**
Van Wyk (2016) (318)	**√**	**√**	**√**	**?**	**?**	**x**	**?**	**?**	**√**	**√**	**Moderate**

√*, Yes or Methodologically Sound;* ***x****, No or Not Methodologically Sound;* ***?****, Can't tell whether Methodologically sound or not.*

4.5.4 Translation

We identified five key concepts (numbered 1-5 below) encompassing eight sub-themes (underneath these concepts) that reflected the main influences on this decision-making process. These are reported below supported by first-order (italicised quotations) and second-order (non-italicised quotations) interpretations (Greater detail located in Appendix 4)

The complexity of the decision-making process was evident throughout. Overall, *"the aim of improving care"* for residents was a priority (307), but there was tension as to how this was best achieved. The options for managing BPSD were generally perceived to be binary – antipsychotic prescribing or non-pharmacological interventions - with the former option considered to be the *"quick-fix"* (58, 64, 91).

4.5.4.1 1. Organisational Capacity

4.5.4.1.1 Resources and access to services:

Understaffing and insufficient time to engage with residents, to conduct thorough assessments of underlying causes, and perform non-pharmacological interventions was mentioned throughout the reviewed studies: (58, 64, 90, 91, 301, 302, 308, 310, 311, 313, 314, 316-318) *"The greatest impact on good outcomes for behaviour management is time limits. Nurses are always under pressure to hurry" (316)*. In some studies there was a suggestion that medication was used to compensate for poor staffing levels: (91, 317) *"sometimes [it's] easier to give a tablet" (91)*. This understaffing issue was further compounded by a lack of access to specialist services such as psychiatrists, therapists and pharmacists (64, 307, 310, 313, 314).

In some studies, nursing home managers working in the public sector stated that there was very little they could do to solve staff shortages due to the lack of funding (310, 313, 317). Financial issues were a parallel concern in private sector nursing homes, and were associated with the use of antipsychotics as a means to deal with constrained expenditure on staff: (64, 301, 317) *"The desire to make money means that [managers] have to make choices about staffing levels and staffing quality that is good for the money making side but not necessarily good for the patient side… That's where controlling and managing the patient might come in" (317)*.

4.5.4.1.2 Coping with the severity of behaviours:

Many studies reported a struggle to manage residents with severe behavioral problems (58, 64, 301, 311, 312, 318). Nurses reported that they were constantly *"putting out fires"(58)*, causing them to feel "overwhelmed" (317). Prescribers reported that "they had little option but to prescribe" to help relieve these situations (64). Consequently, staff felt they were *"letting the residents down"* (311), thus contributing to poor staff morale (311, 312, 314, 317, 318).

Nursing home staff reported conflicting priorities. Dealing with escalating behavioral issues could be perceived as a barrier to completing other nursing tasks: (58, 302, 311, 316) "Medications were viewed as a resource that allowed nurses… to reduce the agitation and complete daily care tasks successfully"(58).

4.5.4.2 2. Individual Professional Capability

4.5.4.2.1 Skills:

Possessing the necessary skills was considered critical for effective BPSD management (58, 64, 91, 301, 302, 308-318). Staff and family members realised the importance of good interpersonal skills when dealing with residents (308, 312, 318), because approaching residents "in the wrong way" could trigger behavioral symptoms (308), while good interpersonal skills could have a positive effect (308).

There was a belief that some staff, particularly newly qualified healthcare assistants, were not adequately trained to deal with behavioral symptoms (64, 302, 311, 317, 318). Prescribers commented that these deficiencies were contributing towards the pressure to prescribe antipsychotics (64) *"to ensure that there is no colourful behaviour"(317)*.

In some studies, staff appeared unable to effectively apply a range of individualised non-pharmacological interventions to the residents (58, 302, 316). Participants noted that familiarity with the resident, training, sharing of experiences and practice improved their confidence in applying non-pharmacological approaches (58, 302, 311, 313, 315-318).

4.5.4.2.2 Knowledge:

In several studies, both prescribers and staff were perceived to lack adequate knowledge on the risks and benefits of antipsychotics (91, 301, 309, 313, 315, 316), and to lack awareness regarding the nature and range of alternative approaches (58, 64, 302, 310, 313, 315, 316). In one study, prescribers believed nurses and family

members expressed “unfounded high expectations” of the effectiveness of antipsychotics (301), while in other studies, staff felt that it was the prescribers who did not have enough knowledge (91, 310, 313). The authors of one study concluded “that poor staff knowledge of appropriate use of antipsychotics may underlie the high rate of administration, despite the reported limitations to its use”(316).

There was a strong desire by participants for more hands-on, interdisciplinary training and education (58, 302, 310, 311, 313-318), that can “help staff relinquish the need for control in favour of understanding”(302).

Knowing the resident and understanding their individual behaviours was critical to performing person-centred care (58, 90, 91, 301, 302, 307, 308, 311, 312, 316-318). However this took a lot of time, staff consistency and close involvement with the family, which was not always possible (58, 90, 91, 301, 302, 308, 311, 312, 318).

4.5.4.3 3. Communication and Collaboration

4.5.4.3.1 Communication within healthcare teams and with the family:

Effective communication was viewed as an essential component to successful BPSD management (58, 64, 90, 91, 301, 302, 307-314, 317). Good communication between all those involved in the care of residents, with close involvement of the family, promoted a sense of trust and mutual respect (58, 64, 90, 301, 307, 308, 311-314, 317). Listening to concerns and valuing everybody’s opinion was critical (90, 91, 301, 307, 309-311, 317), and participants felt that *“by jointly looking at the problems and by learning from each other… we gained more clarity, much more peace, and also had a significant decrease in prescribed medication”*(301).

Working together, with a shared goal, was perceived to be essential (58, 90, 91, 301, 307, 308, 310, 311, 313, 314, 317). Interdisciplinary medication reviews were good examples of different stakeholders working together to reduce inappropriate antipsychotic use (90, 301, 307, 313).

In contrast, poor communication and collaboration led to sub-standard dementia care (90, 91, 302, 307, 309-313, 316, 317). Staff saw themselves as a *"cog in a wheel"*: if they all worked together everything ran smoothly, but if one person was not pulling their weight, the whole system fell apart (311). One study discussed issues regarding GPs not attending medication review meetings and the subsequent barrier this presented to reducing inappropriate antipsychotic prescribing (90).

4.5.4.3.2 Clarity of Roles and Responsibilities:

There was a sense of uncertainty regarding roles and responsibilities in relation to antipsychotic prescribing, particularly between different care settings (64, 307, 309-311, 313, 316, 317). GPs felt that the responsibility for antipsychotic prescriptions belonged to the hospital physician who initiated them, *"as the psychiatrist started it they will not stop prescribing it"* (310). In some studies, this caused "confusion"(310), which promoted the belief that it was the job of nursing home staff *"to clean up the situation"*(314).

A perception of being a victim of professional hierarchy was raised in several studies (90, 91, 307, 310, 317, 318). In these studies, staff felt unable to question the prescriber in relation to the appropriateness of a prescription (90, 91, 317), due to the existence of "professional norms that were very traditional and hierarchical in nature"(317). However in other studies, it was the prescriber who did not feel

empowered to say no to a request from nurses (64, 301, 307, 310, 317), because *"they [nurses] want it and it's very difficult to refuse"*(307).

4.5.4.4 4. Attitudes towards people with dementia and the management of BPSD

4.5.4.4.1 Personal Attitudes:

Attitudes towards antipsychotics were on a spectrum (58, 91, 301, 302, 307-312, 314, 316, 318, 319), ranging from being viewed as *"really beneficial" (91)* to *"chemical cosh"(309)*. Participants in some studies were concerned by their usage and believed the side-effect profile to be unacceptable (58, 64, 90, 301, 302, 308, 309, 311, 314, 316-318). Other participants had a more *"pro medicine"* attitude (58), and it appeared that they might have used antipsychotics for convenience (58, 91, 302, 311).

Participants in several studies believed that antipsychotics were required for the greater good (58, 302, 317). GPs in one study considered the potentially serious side effects "a worthwhile trade-off" if they improved residents' quality of life (310), and in another study perceived them as a *"necessary evil"* to help staff deal with their high workload (317).

Participants generally held positive views towards people with dementia (58, 308, 311, 317, 318) and "expressed great empathy with residents"(318). However participants in some studies voiced dismissive attitudes towards people with dementia (91, 311, 312, 317, 318), and expressed a desire to manage the resident rather than assess the underlying cause (64, 91, 301, 302, 309, 311, 317). In one study, a staff member stated that they found residents' behaviours *"annoying"* (91).

Fear of behaviour recurrence was expressed in several studies (301, 307, 309, 311, 312, 318), hence "there can even be resistance from nurses and family to withdraw [antipsychotics], especially when considerable effort was put into stabilising the [behaviours]"(301).

4.5.4.4.2 Organisational and Societal Attitudes:

The pressure to prescribe from nursing homes was a key finding in a number of studies (58, 64, 90, 91, 301, 307, 310, 317). One GP admitted that this pressure to prescribe forced them to withdraw their medical services to a particular nursing home as they felt it was at odds with evidence-based practice (317).

Managers were seen to play a key role in communicating messages about best practice (90, 308, 311, 317, 318). Managers that emphasised the value of non-pharmacological approaches created a culture where alternative approaches were exhausted before antipsychotics were used. One pharmacist observed that: *"If the attitude's right at the top, then it filters through. If you have management that don't really do the right thing or don't really care, then that filters through as well"(317)*. In most studies management culture was highlighted as a driver of the quality of healthcare provided (58, 90, 91, 302, 308, 311-313, 315-318).

4.5.4.5 5. Regulations and Guidelines:

Regulations and guidelines produced mixed reactions (64, 90, 301, 302, 310, 313, 314). Regulations were perceived as the "driving force" for improving standards in nursing homes (302), but prescribers expressed "ambivalence" towards the influence of guidelines (301).

Regulations were only mentioned in studies conducted in the US (302, 313-315) and Australia (90). According to one US study author: "regulatory oversight has altered the landscape"(302). In Australia, although the conduct of pharmacist-led medication reviews were mandatory for residential settings, there was great variability between nursing homes in how the resultant recommendations were utilised (90).

Guidelines were perceived to be less influential with regards to changing antipsychotic prescribing (64, 301, 310). In one study, prescribers felt that guidelines were unhelpful as they often contradicted their own clinical experience and caused *"more problems" (64)*. Prescribers from another study argued that some guidelines could be interpreted to allow for greater levels of prescribing (301). "What was more influential was past experience of a drug, although guidelines… were taken into account" (64).

4.5.5 The Impact of Context on Findings

The professional background of the research team of included studies tended to influence the focus of inquiry of included studies. In general, researchers from a nursing or social science background tended to focus on the person with dementia, in an attempt to understand these behavioral issues: (58, 302, 308, 309, 311, 312, 318) *"they're frustrated because they can't explain how they're feeling"(308)*. Whereas researchers from a medical or pharmacy background tended to focus on more structural (e.g. resources) or organisational (e.g. interprofessional relationships) issues: (64, 90, 301, 307, 310, 313-315, 317) "*homes are dealing with a greater level of illness and disturbance than they were designed for"* (64). However there were some contradictions and not every study followed this pattern (91, 316).

Furthermore, the majority of included studies explored both perspectives to varying degrees (58, 90, 91, 301, 302, 308-311, 314, 316-318).

Time has also impacted on the findings. The earliest of these studies, published in 2003, discussed antipsychotics as an option for BPSD management, without necessarily attributing positive or negative connotations to this practice (312). However studies published since (2007-2016), have generally advocated a more cautious approach (58, 64, 90, 91, 301, 302, 307-309, 311, 313-318). This is possibly due to the publication of a meta-analysis in 2005 providing evidence of the risks associated with antipsychotic prescribing in people with dementia (112).

4.5.6 Synthesis

Synthesising these first- and second-order interpretations resulted in 20 distinct third-order interpretations. Consequently, each key concept was linked to multiple third-order interpretations; Organisational Capacity (n=5), Individual Professional Capability (n=4), Communication and Collaboration (n=3), Attitudes (n=6) and Regulations and Guidelines (n=2). These third order interpretations, and the CERQual confidence levels associated with them are summarised in **Table 9**. There were eight third-order interpretations in which we have high confidence. Therefore, we believe it is highly likely that these third-order interpretations are reasonable representations of the phenomenon of interest.

Table 9: CERQual Summary of Qualitative Findings

Review finding/Third-Order Interpretations	Relevant papers	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Organisational Capacity			
1. Chronic under-staffing is a fundamental issue in Nursing Homes, leading to insufficient time and ability by Nursing Home staff to perform person-centered care.	(58, 64, 91, 301, 302, 310, 311, 313, 316-318)	**High confidence**	Minor concerns regarding methodological limitations and adequacy
2. The involvement of specialist services can influence antipsychotic prescribing, but there can sometimes be difficulty accessing these services.	(64, 90, 301, 302, 310, 313-317)	**High confidence**	Minor concerns regarding methodological limitations, coherence and adequacy.
3. To circumvent the problems of inadequate resources and/or poor access to specialist services, antipsychotics are 'employed' as cheap, fast and effective staff members.	(64, 91, 301, 302, 310, 311, 313, 314, 316, 317)	**High confidence**	Minor concerns regarding methodological limitations and adequacy.
4. As behaviours escalate, a 'tipping-point' is reached, after which an urgency to resolve the situation arises. This is particularly true when Nursing Home staff feel "overwhelmed" by these behaviors. In these situations antipsychotics are perceived by Nursing Home staff to offer a "more guaranteed result".	(58, 64, 301, 302, 311, 312, 317)	**Moderate confidence**	Minor concerns regarding methodological limitations. Moderate concerns regarding adequacy
5. The perceived acuteness of situations forces Nursing Home staff to focus their attention on the "aggressive" residents, while the "passive" ones are left behind. Antipsychotics can sometimes be viewed as a way of equalising attention given to both "passive" and "aggressive" residents.	(58, 301, 302, 311, 316-318)	**Low confidence**	Minor concerns regarding methodological limitations. Moderate concerns regarding coherence and adequacy
Individual Professional Capability			
6. Both prescribers and Nursing Home staff are often perceived to be poorly equipped to deal with BPSD in terms of deficiencies in dementia-specific skills and/or a lack of knowledge on the risk/benefits of antipsychotics, and the range and nature of non-pharmacological interventions. These deficiencies enable inappropriate antipsychotic prescribing.	(58, 64, 91, 301, 302, 309, 310, 312-318)	**Moderate confidence**	Minor concerns regarding methodological limitations and relevance. Moderate concerns regarding coherence
7. More training and education to help prescribers and nursing home staff to improve skills and knowledge with regards to BPSD management is desired.	(58, 301, 302, 311, 313-318)	**High confidence**	Minor concerns regarding methodological limitations
8. Even in individuals with sufficient skills and knowledge regarding BPSD management, a tension can exist between 'doing the right thing' and doing what's practical, especially if the resources or suitable alternatives are not perceived to be there to support adequate implementation.	(58, 64, 90, 91, 301, 302, 311, 313, 317, 318)	**Moderate confidence**	Minor concerns regarding methodological limitations and coherence. Moderate concerns regarding adequacy.

9. Knowing the resident and understanding their behaviours contributes towards successful BPSD management.	(58, 64, 91, 301, 302, 308, 311, 312, 317, 318)	**High confidence**	Minor concerns regarding methodological limitations and adequacy.
Communication and Collaboration			
10. Effective communication and collaboration (involving sharing information and listening to others) between all members of the healthcare team are key enablers to reducing inappropriate prescribing of antipsychotics. The involvement of family members can also be important in this process.	(58, 64, 90, 91, 301, 302, 307-315, 317)	**High confidence**	Minor concerns regarding methodological limitations, coherence and relevance
11. A lack of empowerment at all levels of the healthcare team and among family members is a barrier to informed decision-making regarding antipsychotic prescribing.	(58, 64, 90, 91, 301, 307-313, 317, 318)	**High confidence**	Minor concerns regarding methodological limitations, coherence and relevance.
12. Fragmentation between different levels of care creates confusion surrounding roles and responsibilities, which can lead to inappropriate maintenance of antipsychotics.	(64, 90, 302, 307, 309, 310, 313, 314)	**Moderate confidence**	Minor concerns regarding adequacy. Moderate concerns regarding methodological limitations
Attitudes towards people with dementia and the management of BPSD			
13. Although there is a preference to use non-pharmacological interventions in the first instance due to the unpleasant side effects of antipsychotics, it is acknowledged that antipsychotics are a "necessary evil" and are often unavoidable.	(58, 64, 90, 91, 301, 302, 308-314, 316-318)	**Moderate confidence**	Minor concerns regarding methodological limitations and relevance. Moderate concerns regarding coherence.
14. Negative attitudes by individuals towards people with dementia can result in inappropriate antipsychotic prescribing. Conversely, empathy towards people with dementia can be protective.	(58, 90, 91, 301, 302, 308, 309, 311, 312, 316-318)	**Moderate confidence**	Minor concerns regarding coherence, relevance and adequacy. Moderate concerns regarding methodological limitations
15. Fear of the recurrence of behaviours motivates maintenance of antipsychotic prescribing.	(58, 301, 307, 309, 311, 312, 317, 318)	**Low confidence**	Minor concerns regarding relevance. Moderate concerns regarding methodological limitations and adequacy
16. Organizational and societal attitudes towards people with dementia and the management of BPSD, exerts pressure on prescribers to make prescribing decisions.	(58, 64, 90, 91, 301, 302, 307-311, 317)	**High confidence**	Minor concerns regarding methodological limitations and coherence.
17. The attitude of the nursing home manager towards people with dementia and the management of BPSD dictates the treatment culture of that nursing home, and this has a strong influence on antipsychotic prescribing.	(58, 90, 91, 308, 311, 313, 317, 318)	**Moderate confidence**	Minor concerns regarding methodological limitations. Moderate concerns regarding adequacy
18. Tensions can arise due to incompatible beliefs towards antipsychotics between prescribers and nursing homes; in these cases a battle of wills develops where there is often pressure on prescribers to "do something" in order to restore control – doing nothing is not tolerated. However, sometimes	(64, 90, 91, 301, 307, 310, 311, 313, 317)	**Moderate confidence**	Minor concerns regarding methodological limitations. Moderate concerns regarding adequacy

there is pressure on prescribers to discontinue antipsychotics, to which there can be resistance from prescribers.			
Regulations and Guidelines			
19. Regulations are perceived to be the driving force for antipsychotic reductions in nursing home residents with dementia, but adherence to them can be challenging.	(90, 302, 313-315)	**Very low confidence**	Moderate concerns regarding methodological limitations. Substantial concerns regarding adequacy
20. Guidelines exert little influence on antipsychotic prescribing, but may act indirectly to increase knowledge regarding the risk/benefits of antipsychotics.	(64, 301, 310)	**Very low confidence**	Moderate concerns regarding methodological limitations. Substantial concerns regarding adequacy

BPSD, Behavioural and Psychological Symptoms of Dementia; CERQual, Confidence in the Evidence from Reviews of Qualitative Research.

By linking all 20 third-order interpretations together we developed a *'line of argument'*, which is outlined below and expressed as a conceptual model in **Figure 20**. This conceptual model describes the process of a dysfunctional negative feedback loop where any *'challenging behaviour'* in a person with dementia promotes either antipsychotic prescribing or a non-pharmacological intervention, or sometimes both, all with the goal of suppressing the *'challenging behaviour'* and restoring calm. The *'challenging behaviour'* may push decision-making towards an exclusively pharmacological solution, especially if staff feel overwhelmed. Once the *'challenging behaviour'* is suppressed, the need for an intervention is reduced. However, the fear that these behaviours may return at any time, or confusion surrounding roles and responsibilities facilitates maintenance of antipsychotic prescribing, breaking the feedback loop.

The five key concepts, and eight sub-themes described above, act as the overarching influences on this decision-making process as a whole. The conceptual model illustrates that some or all of these influences may come into play when a *'challenging behaviour'* arises (**Figure 20**). These influences interact with each other, often in an unpredictable and complex manner, and ultimately determine the response behaviours from staff.

Our synthesis indicates that different stakeholders struggle to see things from other stakeholders' perspective and do not acknowledge the pressure the others are under. However, when all stakeholders come together to communicate and collaborate as equal and empowered partners the inappropriate use of antipsychotics can be reduced.

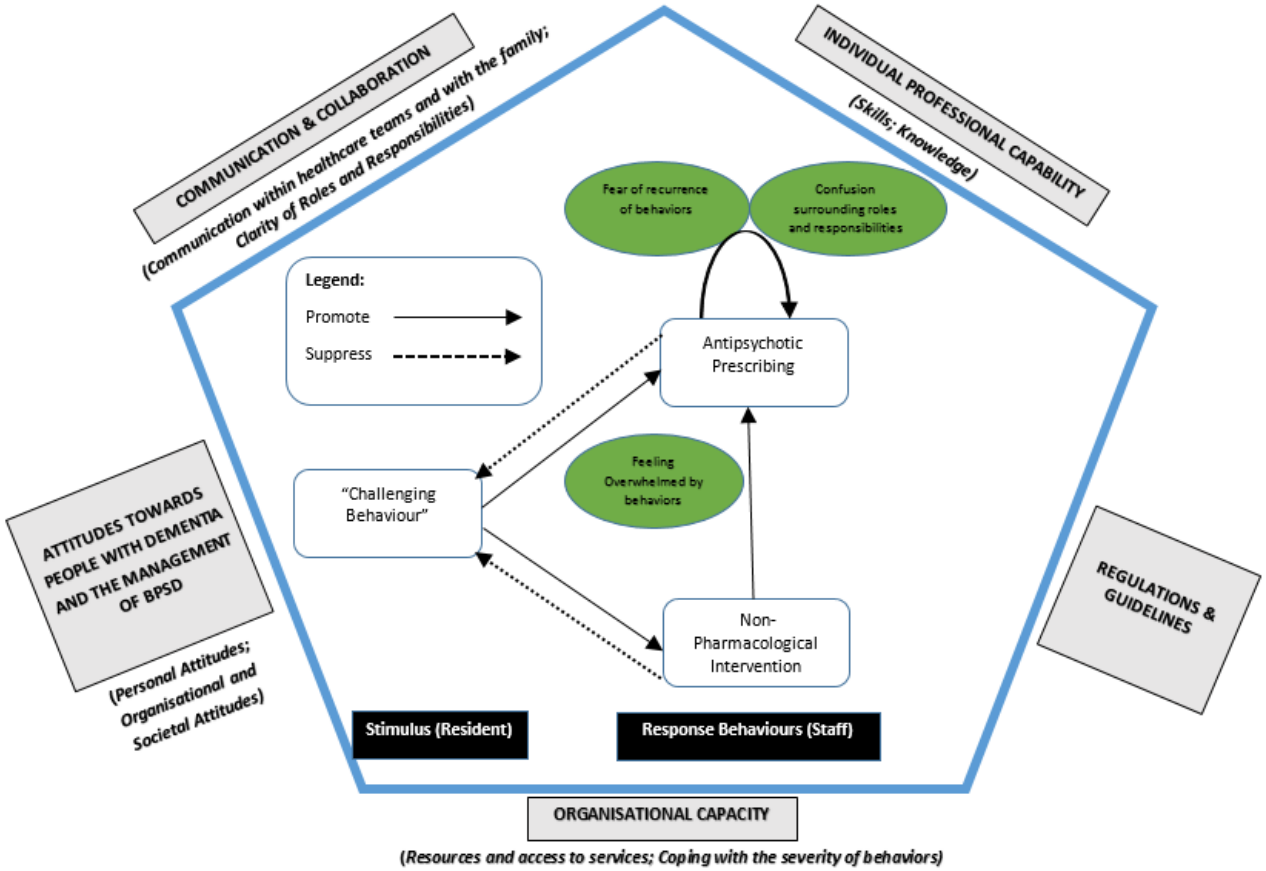

Figure 20: Conceptual Model of Influences on Decision-Making Regarding Antipsychotic Prescribing in Nursing Home Residents with Dementia

Key concepts are in shown in CAPITALS; sub-themes are in (italics) beneath the relevant key concept; and specific factors influencing response behaviours are in green circles. All influences can impact upon the decision-making process at the core of this diagram. BPSD, Behavioural and Psychological Symptoms of Dementia

4.6 Discussion

This study is the first to our knowledge, to systematically review and synthesise the qualitative evidence surrounding antipsychotic prescribing in nursing home residents with dementia. Additionally, we believe that this study is the first to apply CERQual to a meta-ethnography. Our findings highlight the complexity of this topic and the various influences on decision-making. We have conceptualised these influences in a *'line of argument'* that moves beyond the findings of the individual studies, as a dysfunctional negative feedback loop, which we believe will be useful for clinicians, researchers and policy-makers.

4.6.1 Comparison with Previous Research

A systematic review exploring the quantitative relationship between facility characteristics and antipsychotic usage concluded that in general, as nursing staff levels decrease, antipsychotic usage increases (320). The authors also reported a positive association between for-profit nursing homes and antipsychotic usage (320). However these associations are not always clear-cut (92, 321-323). The focus on qualitative evidence in our review helped us to tease out these more complicated elements. Our findings reinforce that nursing homes are struggling with understaffing and poor access to important services. Consequently, staff can become overwhelmed by behaviours in these resource-poor environments. Nursing home managers, particularly in the for-profit sector, may be tempted to use antipsychotics as a more economical solution to the problem. However it is important to

acknowledge that the use of antipsychotics as a cost-saving measure appeared in not-for-profit nursing homes also.

Knowledge of the risks and benefits of prescribing antipsychotics in dementia has been found to be quite variable, and often suboptimal (324-326). Some authors have commented that these deficits in knowledge may be contributing to a concerning belief that antipsychotics are highly effective for BPSD (324, 325). Furthermore, staff have often been found to be inadequately trained in person-centred care (324, 325, 327). Our findings suggest that inadequate skills and knowledge are enabling inappropriate antipsychotic prescribing. Even in highly capable individuals, we found a tension between doing the *'right thing'* and doing what's practical, given resource limitations and their duty of care to other residents.

Previous research has found that communication breakdown is an impediment to the delivery of person-centred care (328), and is also a barrier to deprescribing (329). Professional hierarchies in the nursing home setting have previously been reported as a barrier to evidence-based practice (328, 330, 331). Furthermore, GPs have expressed frustration at the lack of communication from hospital consultants with regards to the management of antipsychotics (332), as well as the pressure to prescribe from nursing homes (325). Our findings add to this knowledge by identifying a lack of empowerment at all levels of the healthcare team and among family members as a barrier to informed antipsychotic prescribing decision-making.

The concept of *'treatment culture'* in nursing homes has been discussed in the literature in an attempt to explain why certain nursing homes continue to have high levels of antipsychotic prescribing independent of residents' clinical characteristics

(333-335). Treatment culture can be defined as the *"beliefs, values, and normative practices associated with medication prescribing and administration"* (334). Nursing homes with a traditional culture (i.e. rigid routines) have been associated with higher levels of antipsychotic prescribing than those with a resident-centred culture (i.e. person-centeredness) (334). Our research confirms this notion of treatment culture and the impact of conformity on prescribing decisions. Our findings add to existing evidence by highlighting the important role of the manager, who can diffuse a philosophy of person-centred dementia care throughout the organisation (62).

Our findings indicate that an underlying fear of behaviour recurrence may be one factor driving the desire for control. Negative connotations of dementia have been described in the literature, comparing the effect BPSD has on people to becoming *"dehumanised"* (49). Based on the findings of our review, we believe that a lack of understanding of the nature and progression of dementia can lead to the inappropriate maintenance of antipsychotics.

4.6.2 Implications

The conceptualisation of decision-making as a dysfunctional negative feedback loop with the ultimate aim of controlling residents, challenges us in the way we perceive dementia. We need to re-frame the way we view so-called *'challenging behaviours'*. These behaviours may not necessarily be challenging to the person with dementia – only to us. There have been discussions surrounding the nuances of terminology in this area, with a term such as *'responsive behaviours'* being preferable (34). There needs to be an appreciation that these behaviours are generally due to some unmet need (336), and often do not respond to antipsychotics (337, 338). Therefore it is

imperative that interdisciplinary training and education is delivered to all involved in the care of residents with dementia, including family members.

Furthermore, communication structures and interdisciplinary practices need to be optimised in order to improve the flow of vital information. It is important that peripheral members of this interdisciplinary team are not excluded from decision-making as they can often hold the key to successful behavioral management. There is also evidence to support the inclusion of pharmacists in these teams (151). Shared decision-making, a collaborative process that allows people with dementia, family members, and their healthcare team to make healthcare decisions together, should be encouraged (339). Shared decision-making takes into account the best clinical evidence available, as well as values and preferences of the person with dementia and the family (340).

Our CERQual assessments identify areas that policy-makers can potentially target. For instance, policy-makers need to carefully re-examine resource allocation issues, as we have high confidence that nursing homes are utilising antipsychotics to substitute for inadequate resources and poor access to specialist services. Given that the use of antipsychotics in this population is not evidence-based, it is concerning that these agents are being used to cut costs. Therefore in light of the strength of our evidence, we argue that increasing the staff to resident ratio, or increasing access to services, may possibly result in a reduction in inappropriate antipsychotic prescribing.

We now have a greater understanding of this complex prescribing behaviour. However it is still unclear how it can be sustainably changed (151). Behaviour change

interventions need to be guided by the best available evidence and appropriate theory (164). Important contextual issues unique to each healthcare system need to be explored before pilot studies can be conducted (163). More primary qualitative research is needed, focusing on aspects that are currently under-researched e.g. influence of national regulations. It is also crucial that the voice of the person with dementia is ethically and meaningfully included, either as participants of research (341) or as co-researchers in the intervention design process (342). Additionally, our conceptual model identified specific influencing factors, such as confusion surrounding roles and responsibilities, and fear of behaviour recurrence. These identified factors may be suitable for future targeted interventions.

We believe that the interdisciplinary and interdependent nature of this decision-making process is such that it is unlikely that targeting a single stakeholder group will result in any sustainable change in prescribing behaviours. Therefore, we argue that a holistic, person-centred approach to behaviour change is required, involving both the prescribers and requesters of antipsychotics.

4.6.3 Strengths and Limitations

The main strength of our study is its robustness (294). Measures were put in place to ensure the high quality of the analysis including maintaining reflexivity, utilising independent multiple analysts and transparency through careful adherence to the PROSPERO protocol. The study was conducted by an experienced multidisciplinary team. Consequently, we believe that our included studies were analysed to a high standard and the resultant conceptual model provides the reader with a rich, in-depth and valid new interpretation of a complex phenomenon.

Another strength was the great number and diversity of healthcare professionals and family members represented in the included studies. The multiple perspectives allows for a more holistic view of the factors influencing this complex phenomenon.

A limitation of our study, which is true of all systematic reviews of qualitative evidence, is the difficulty retrieving qualitative research from databases. Unlike RCTs, qualitative research has historically been inconsistently indexed in databases, preventing comprehensive and reproducible searches (343). Therefore it is possible that we may have missed a potentially relevant study. However, as our team conducted a systematic and thorough search, which was transparently reported, we are reasonably confident that we have captured all relevant studies.

4.7 Conclusion

Antipsychotic prescribing in nursing home residents with dementia occurs in a complex environment involving the interplay of various stakeholders (with differing levels of skills and knowledge, who often have conflicting views on the role of antipsychotics and who may not be equally empowered), the nursing home organisation (with its own treatment culture and level of resources) and external influences (such as guidelines, regulations and societal influences). In order to improve the quality of antipsychotic prescribing in this cohort, a paradigm shift is required towards a more holistic approach to BPSD management. While we have found the issue of antipsychotic prescribing has been extensively explored using qualitative methods, there remains a need for research focusing on how best to change the prescribing behaviours identified. It is also crucial that the voice of the

person with dementia is ethically and meaningfully included in such research, either as participants of research or as co-researchers in the intervention design process.

4.8 Addendum

4.8.1 Updated Search Results

An updated search of the electronic databases was conducted on July 11th 2018 to search for all potentially relevant articles published since July 2016 (date of latest search prior to publication). A total of 906 records were identified. After duplicate removal, 398 records were screened by title and abstract and 15 full-text articles were subsequently assessed for eligibility. This resulted in nine new published articles meeting our inclusion criteria and hence were included in our updated systematic review (344-352). Furthermore, three additional articles which were manually located (353-355), also met our inclusion criteria, bringing our updated systematic review to a total of 12 new studies, and 30 studies overall (**Figure 21**).

The characteristics of these 12 studies are outlined in **Table 10** below. In brief, these 12 studies include 623 unique participants from nine new study cohorts. Three of these new studies used the same dataset of 28 participants (344, 346, 347), while another study (351) used the same dataset of 40 participants that were previously included in two studies from our original search (90, 317). As before, no study included people with dementia as research participants. The 12 studies were conducted in five different countries: UK (n = 4), US (n = 4), Australia (n = 2), Canada (n = 1) and Ireland (n = 1).

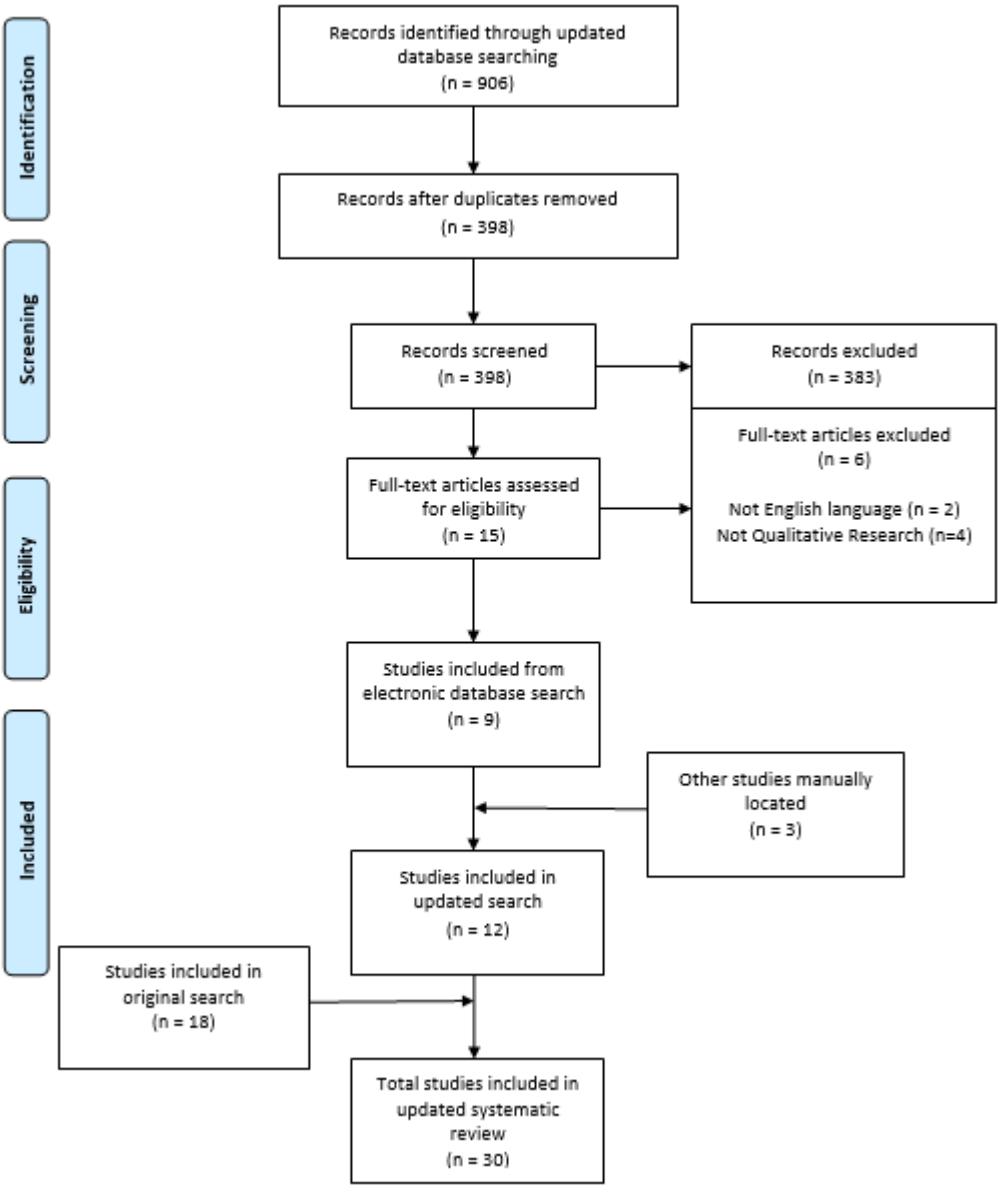

Figure 21: PRISMA flow diagram of updated search strategy results

Table 10: Characteristics of Included Studies from the Updated Search

First Author	Year of Publication	Country	Study Objectives	Methods	Data Collection	Qualitative Data Analysis	Participant characteristics (n)	Setting (n)
Birney (353)	2016	Canada	To determine how interprofessional collaboration was incorporated in the antipsychotic medication reviews and how the reviews had been sustained	Q	Semi-structured interviews and observations	Thematic Analysis	Healthcare assistants (5), Registered nurses (3), Licensed practical nurses (3), Pharmacists (4), Best practice lead (1), Care manager (1), Facility Director (1). Total participants (18)	LTC facilities (4)
Donyai (346)	2017	UK	To explore the use of fallacious arguments in professionals' deliberations about antipsychotic prescribing in dementia in care home settings	Q	Semi-structured interviews	Content Analysis	Psychiatrists (5), Geriatricians (2), GPs (5), Care home managers (5), Community psychiatric nurses (7), Primary-care pharmacists (2), Memory-clinic nurse (1), Social worker (1). Total participants (28) **‡[1]**	GP practices, care homes and hospitals (unknown number) **§[1]**
Gill (347)	2017	UK	To explore professionals' deliberations about antipsychotic prescribing in dementia using critical discourse analysis within a social constructionist approach	Q	Semi-structured interviews	Discourse Analysis	Psychiatrists (5), Geriatricians (2), GPs (5), Care home managers (5), Community psychiatric nurses (7), Primary-care pharmacists (2), Memory-clinic nurse (1), Social worker (1). Total participants (28) **‡[1]**	GP practices, care homes and hospitals (unknown number) **§[1]**
Simmons (355)	2017	US	To explore nursing home staff perceptions of antipsychotic medication use and identify both benefits and barriers to reducing inappropriate use from their perspective	Q	Focus Groups	Hierarchical coding system	Licensed practical nurse (11), Registered nurse (4), Social worker (4), Facility administrator (2), Nurse practitioner (2), Director of nursing (2), Certified nursing assistant (2), Assistant director of nursing (1), Mental health intern (1). Total participants (29)	Community nursing homes (3)
Tjia (352)	2017	US	To describe the extent to which nursing homes engaged families in antipsychotic initiation decisions in the year before surveyor guidance revisions were implemented	M	Closed- and open-ended questions in semi-structured interviews	Directed content analysis	Family members of nursing home residents (41)	Nursing homes (20)
Almutairi (344)	2018	UK	To develop an in-depth explanatory model about inappropriate prescribing of antipsychotics in dementia within care homes	Q	Semi-structured interviews	Grounded Theory	Psychiatrists (5), Geriatricians (2), GPs (5), Care home managers (5), Community psychiatric nurses (7), Primary-care pharmacists (2), Memory-clinic nurse (1), Social worker (1). Total participants (28) **‡[1]**	GP practices, care homes and hospitals (unknown number) **§[1]**
Chenoweth (345)	2018	Australia	To identify the contextual elements that the nurse champions considered most critical in facilitating, adhering to and achieving success with the person-centred care component of the HALT intervention, and how this change process impacted on care delivery and	Q	Open-ended survey and semi-structured interviews	Thematic Analysis	Senior registered nurse (6), Clinical nurse specialist (4), Clinical nurse consultant (5), Nurse practitioner (1), Quality manager (3), Deputy director of nursing (1), Care unit manager (2). Total participants (22)	Care homes (24)

			outcomes for participating residents from the champions' perspectives					
Jennings (354)	2018	Ireland	To establish the challenges GPs experience when managing BPSD, to explore how these challenges influence GPs' management decisions, and to identify strategies for overcoming these challenges	Q	Semi-structured interviews	Thematic Analysis	GPs (16). Total participants (16)	GP practices (unknown number) **§[2]**
Kerns (348)	2018	US	To assess experiences and perceptions of family and nursing caregivers regarding factors influencing medication decisions for BPSD	Q	Semi-structured interviews	Template, immersion and crystallisation, and thematic development	Family members of community patients (8), Family members of assisted living patients (7), Family members of nursing home patients (5), Nurses in assisted living facilities (6), Nurses in nursing home (6). Total participants (32)	Mixture of own home (unknown numbers), assisted living facilities (4) and nursing homes (4) **§[2]**
Kerns (349)	2018	US	To evaluate how and why primary-care physicians employ non-pharmacologic strategies and drugs for BPSD	Q	Semi-structured interviews	Template, immersion and crystallisation, and thematic development	Primary care physicians (26) [16 trained in family medicine and 10 in internal medicine]. Total participants (26)	Primary care physician surgeries (unknown number) **§[2]**
Mallon (350)	2018	UK	To determine the views of care home staff in relation to experiencing and managing behaviour that challenges in dementia, and their experiences of training	M	Survey with some open-ended questions	Thematic Analysis	Nurse (69), Care worker with formal qualifications (66), careworker without formal qualifications (15), other worker (38), manager (223). Total participants (411)	Dementia Specialist Care homes (352)
Sawan (351)	2018	Australia	To identify the espoused values of nursing home staff regarding the ideals for the use of psychotropic medicines in residents with behavioural and psychological disturbances, and to uncover why the espoused values are in/consistent with described practices, by exploring the basic assumptions influencing psychotropic medicine use.	Q	Semi-structured interviews	Thematic Analysis	Managers (8), Registered Nurses (8), Nursing Assistants (5), GPs (8), Pharmacists (6), Enrolled nurses (2), Specialist medical practitioner (1), Nurse Practitioner (1), Clinical Nurse Consultant (1). Total participants (40) **‡[2]**	Nursing Homes (8)

Q, Qualitative Methods; M, Mixed Methods; BPSD, Behavioural and Psychological Symptoms of Dementia; NPI, Non-pharmacological interventions; LTC, Long-term care; SCU, Specialist Care Unit; GP, General Practitioner (also known as Primary Care Physicians).

** Study did not obtain specific degree affiliation, thus unable to distinguish between social workers and nursing staff. † Unknown breakdown of participants. §[1] Research participants may not have been based in a Nursing Home Setting, but focus of study is on people with dementia in the Nursing Home Setting. §[2] Research participants may not have been based in a Nursing Home Setting, but a component of study is concerned with people with dementia in the Nursing Home Setting, and we are focusing on this component. ‡[1] The same study cohort in these three studies. ‡[2] The same study cohort as a previously included study by the same authors*

4.8.2 Analysis Methods

A *deductive* framework approach was utilised to explore how well, or otherwise, the findings of these 12 new studies fitted with our original key concepts, sub-themes and *'line of argument'* (356). Using NVivo version 11 (304), the results and discussion sections of each new study were coded according to our predefined concepts, sub-themes and *'line of argument'*, specifically focusing on areas of agreement and disagreement. Where novel concepts emerged these were coded separately (*'other'*), and were explored in detail. We compared our updated findings to our existing conceptual model (**Figure 20**), to assess whether this model remained valid or whether modifications were needed. Importantly, none of the 12 studies cited our published systematic review (3), hence none of these studies are likely to have been biased by knowledge of our findings.

4.8.3 Updated Analysis Results

For the purpose of this update, each of the original key concepts and sub-themes shall be presented in turn, focusing on areas of agreement and/or disagreement with the new findings. Finally we shall comment on how these findings impact on our previously developed *'line of argument'* and conceptual model. As before, these are reported below supported by first-order (italicised quotations) and second-order (non-italicised quotations) interpretations.

4.8.3.1 1. Organisational Capacity

4.8.3.1.1 Resources and access to services:

There was strong agreement from almost all of these studies that under resourcing in nursing homes and inadequate access to specialist services impacted on participants' decision to use antipsychotics (344, 345, 347-355): "*And I think there has to be resource to provide alternative as well because unless there's resource to provide trained carers who can manage behavioural symptoms the default scenario will often be medication"* (344). The authors of this same study concluded that "within busy care homes, the many challenges of BPSD need a solution and the prescribing of antipsychotics provides a mechanism through which the multitude of work can be managed" (344). No study reported any conflicting findings with regards this sub-theme.

4.8.3.1.2 Coping with the severity of behaviours:

Once again there was strong agreement from these studies that antipsychotics were used as a means of coping with BPSD (344, 346-348, 351, 354, 355). One study concluded that "antipsychotic medications were characterised as a tool for managing uncontrollable and disruptive patients who are *"hitting other patients or the staff," "trying to break down the window"* or have *"ripped a radiator of the wall".* In this regard, antipsychotics are portrayed as helpful… within a care-home when faced with an even more harmful option of not being able to deal with an aggressive patient" (347). In this and a related study, the authors describe how participants constructed a *"false dichotomy"* surrounding the binary options of prescribing (to help alleviate the situation) or not prescribing (to let the situation escalate). Hence the prescription

of antipsychotics was considered the *"lesser of two evils"* (346, 347). No study contradicted this sub-theme.

4.8.3.2 2. Individual Professional Capability

4.8.3.2.1 Skills:

Similar to our previous findings, the importance of having the skills to conduct non-pharmacological behavioural management was viewed by participants in these studies as being key to preventing inappropriate antipsychotic usage (345, 349, 350, 354). A lack of training was often seen as a barrier to implementing NPI. In one study, it was reported that "most [GPs] acknowledged they had little formal training in non-medication therapies for dementia", and this impacted on their willingness to recommend them for BPSD (349). Furthermore, the importance of delivering person-centred care training to all nursing home staff was emphasised in several studies as a means of reducing inappropriate antipsychotic usage (345, 348, 350). No study contradicted this sub-theme.

4.8.3.2.2 Knowledge:

Having an appropriate level of knowledge surrounding the limited evidence of antipsychotic benefits and the substantial risks of their use in people with dementia was perceived to be essential in almost all of these new studies (344-350, 352-355). In one study which explored participants' experiences of an intervention aimed at delivering education and support to nursing home staff, one participant commented on the perceived benefits of increased knowledge; "*I think the project has created awareness that antipsychotic medications are dangerous and not always the answer. It has allowed staff to witness first-hand the behaviours of residents who have been*

successfully deprescribed. It has shown that it is a myth that behaviours automatically increase when antipsychotic medications are decreased" (345).

However one study suggested that it was confidence (that comes from experience) rather than purely knowledge that was more important in determining how GPs managed BPSD; "This confidence influenced their management, making them more willing to engage in trial prescribing, more cognisant of avoiding crisis presentations and more aware of their own limits" (354). One GP participant from this study stated that: *"What I've learnt… is that you 'give it as a trial' and sometimes it's absolutely bingo and sometimes it bounces off and you move off it pretty quickly and try the next one."* Interestingly though, the authors reported that for GPs "this confidence did not seem to extend to non-pharmacological management strategies" (354).

4.8.3.3 3. Communication and Collaboration

4.8.3.3.1 Communication within healthcare teams and with the family:

Communication and teamwork involving all members of the interdisciplinary team with close involvement of family members was found to be important in reducing inappropriate antipsychotic prescribing, in almost all included studies (344, 345, 348-355). Birney *et al.* observed that "work dynamics and processes… enabled effective [interprofessional collaboration] in the [antipsychotic] medication review. Staff engaged in collaborative decision-making by participating and being respectful of other members' participation. Participants noted effective working relationships with other team members. Also, the participants were clear that different professional groups add another perspective to an issue" (353). One nurse participant from this study stated that: *"It is interdisciplinary, we have people from*

various disciplines. We have health care aides, LPNs [licensed practical nurses], RNs [registered nurses], management and physiotherapists. The medications we deal with affect every department in one way or another. Each discipline will see the patient in a different way than another" (353). No study contradicted this sub-theme.

4.8.3.3.2 Clarity of Roles and Responsibilities:

The importance of having clear roles and responsibilities was discussed throughout (344, 346, 347, 351, 353-355). One study discussed how in an interdisciplinary setting, a clear understanding of roles and responsibilities helped to reduce inappropriate antipsychotic prescribing in residents (353). In another study, the challenges presented when caring for residents across different settings, and hence roles and responsibilities were not clear, were also discussed; *"What tends to happen with antipsychotics are people come in [to the hospital] with delirium and I [a psychiatrist] put them on an antipsychotic, not for BPSD, this is for delirium. And then they get discharged [to the nursing home] after about say seven, ten days. I think the problem arises when the antipsychotic never gets stopped because the GPs just let it continue"* (344). No study contradicted this sub-theme.

4.8.3.4 4. Attitudes towards people with dementia and the management of BPSD

4.8.3.4.1 Personal Attitudes:

There was a strong consensus among included studies that personal attitudes, specifically towards the management of BPSD had a significant influence on antipsychotic decision-making (344-350, 352-355). Family members' attitudes towards antipsychotics were found to be important in determining prescribing decisions, especially if there was a perceived reluctance to deprescribe for fear of

behaviour recurrence. Simmons *et al.* reported that "family attitudes and/or beliefs in which they are either reluctant or opposed to reducing or withdrawing an antipsychotic medication were discussed as a major barrier to making changes" (355). One nursing home staff participant in this study explained why there can be resistance from certain family members: *"Sometimes, families do not want the resident to come off of a medication because they've been on it for so long. They don't want to upset the apple cart, so to speak, so they don't want to change anything"* (355).

However a new concept which emerged in one of these studies which was not reported in any of the original studies was the idea that some family members were fully trusting of prescribers, and did not appear to have an opinion on antipsychotics, one way or the other (352). In this study "some family members had a hands-off, *"doctor knows best about medications"* attitude toward the antipsychotic decision," hence explaining why some family members were happy to not get involved in these types of decisions (352).

4.8.3.4.2 Organisational and Societal Attitudes:

The influence of organisational and societal attitudes were discussed in several studies and were largely in agreement with our original findings (344-347, 351, 354, 355). In particular the pressure on GPs to inappropriately prescribe antipsychotics from nursing homes was explored (344, 346, 347, 351, 354). A GP participant from one study discussed this challenging issue: *"Doctors are prescribing this stuff (psychotropic medicines) all the time inappropriately pressured by these organisations …. I don't want to sell my soul. The minute I do something that I don't*

feel is morally correct because it's going to make life easier for me or just easier when it's not right, I fear that my morality is compromised so I hold very fast to that" (351). No study contradicted this sub-theme.

4.8.3.5 5. Regulations and Guidelines:

The influence of regulation and guidelines on decision-making was more prominent in these newer studies, being discussed in 9 of the 12 studies (344, 346, 347, 349-355). In line with our previous findings, the changing regulatory landscape was discussed in several studies e.g. "consistent with federal regulations, participants commented that efforts are made to avoid a newly prescribed antipsychotic medication whenever possible, particularly PRN antipsychotic use" (355). However, these regulations were sometimes viewed negatively as a way of keeping *"administration happy",* and improving their nursing home star rating (355) rather than for the benefit of the resident and there were some unintended negative consequences reported which did not emerge in earlier studies. For example, in one study there was a suggestion that residents with dementia were having their diagnoses amended to include *"some element of psychosis… [Because] you can't use Alzheimer's dementia to get Seroquel® [quetiapine] covered in the nursing home"* (349). Furthermore, the GPs "also reported increasing their use of other medications that had rarely been used for dementia symptoms" in place of antipsychotics (349).

In relation to guidelines, some of these studies reported that participants were dissatisfied with guidelines for BPSD and found them unhelpful (344, 346, 347, 349), in line with our previous findings. However, some studies reported that participants sought practical guidelines that supported prescribers and offered advice on

medication options: *"It would be nice instead of having all of our guidelines say 'don't do, don't do, don't do,' it'd be nice to find out what we can do"* (349).

4.8.3.6 'Line of argument'

Our original *'line of argument'* visualised as a conceptual model (**Figure 20** above), describes the process of a dysfunctional negative feedback loop where any *'challenging behaviour'* in a person with dementia promotes either antipsychotic prescribing or a non-pharmacological intervention, or sometimes both, all with the goal of suppressing the *'challenging behaviour'* and restoring calm. The 'challenging behaviour' may push decision-making towards an exclusively pharmacological solution, especially if staff feel overwhelmed. Once the *'challenging behaviour'* is suppressed, the need for an intervention is reduced. However, the fear that these behaviours may return at any time, or confusion surrounding roles and responsibilities facilitates maintenance of antipsychotic prescribing, breaking the feedback loop.

We argue that our *'line of argument'* remains valid in light of these new studies. One study in particular which we feel strengthens our argument is Donyai *et al.* who describe the concept of a *"false dichotomy"* whereby the binary options of a) prescribing antipsychotics or b) not prescribing antipsychotics, are framed in such a way that the perceived benefit of prescribing would always outweigh the substantial risk of not prescribing (346). Furthermore, Sawan *et al.* describe the "locus of control and necessity for efficiency or comprehensiveness" in participants, which could help to explain the motivations of individuals in our conceptual model e.g. a sense of helplessness in staff may trigger a request for an antipsychotic in order to restore a

sense of calm (351). Moreover the fear of behaviour recurrence as a rationale for inappropriate antipsychotic maintenance, has been discussed in several studies (344-346, 348, 355).

However, we found some novel concepts in these studies (coded as *'other'*), that suggests that our conceptual model may require some modifications. These two new concepts are *'Different pathways for different residents'* and *'Treatment goals'*. In terms of the former concept, Simmons *et al.* described "three primary antipsychotic prescribing pathways, which lead to specific management strategies" (355). The three different pathways are

1. Admitted on antipsychotics
2. Psychiatric diagnosis
3. Disruptive and dangerous behaviours

The authors argue that the management approaches for these different populations may be different (355). Reflecting on our own conceptual model (**Figure 20**), it is clear that this model more closely resembles that of the third pathway (disruptive and dangerous behaviours). Our model may need to be slightly modified to encompass the possibility that residents may also be admitted on antipsychotics or have a pre-existing psychiatric diagnosis.

In terms of *'treatment goals'*, there was a wider variety mentioned in the newer studies:

- improvement in quality of life and well-being (345, 348, 349, 353, 355)
- reduction in symptom distress (345, 347-349)

- reduction in behaviours (345, 347, 349, 355)
- improvement in alertness (345, 353, 355)
- reduction in antipsychotic usage (353, 355)
- reduction in falls (353, 355)
- improvement in functional status (345, 349)
- improvement in safety (349)
- palliative care goals (348)
- improvement in person-centred care (351)
- improvement in family satisfaction (355)
- improvement in regulatory compliance (355)
- reduction in medication cost (353)

Of note quality of life was seen as possibly the most important goal of treatment: *"The focus should be on quality of life, not numbers. The benefit to a human being is bigger than any cost or number"* (353). This is in contrast to earlier studies, and hence our conceptual model **Figure 20**, where the main goal of treatment appeared to be reduction or elimination of these *'challenging behaviours'*. Therefore it is evident that slight modifications to our conceptual model may be necessary to factor in these evolving preferences in treatment goals for residents with BPSD.

4.8.4 Discussion

In total, 12 studies were included in our updated systematic review, the findings of which were found to strengthen our original key concepts, sub-themes and *'line of argument'.* There has been an exponential increase of publications in this area in a relatively short period of time (from a single paper published in 2003, to 7 papers

published in the first six months of 2018 alone), indicating an increasing interest in this topic. In particular, there has been a greater focus on the influence of regulations and guidelines on decision-making since our initial search, highlighting the rapidly changing regulatory and policy landscape. This systematic review successfully collated these studies and provides clinicians, researchers and policy-makers alike with an up-to-date overview of the influences on decision-making in this complex area of healthcare.

Reflecting on some of the novel concepts emerging from these new studies, there may be a requirement for us to slightly modify our *'line of argument'* and conceptual model, based on developments in participants' understanding of inputs (i.e. different types of residents) and outputs (i.e. goals of treatment) into this complex decision-making process. To help us develop and validate this updated *'line of argument'* and conceptual model, *'member checking'* - asking authors of all included studies for feedback on the developing synthesis - may be helpful (357). This approach was successfully conducted in another meta-ethnography (296).

Due to time constraints, the searches and data extraction for the updated search were conducted solely by the primary researcher. Furthermore, no grey literature searching, no quality appraisal and no CERQual assessments were conducted for this updated search. Hence it is possible that important studies were unintentionally omitted from this updated search, that the new studies may be methodologically flawed and that the confidence in our individual review findings may have changed. Therefore, I recommend that an updated systematic review be conducted, involving multiple reviewers, prior to dissemination of the updated findings.

Chapter 5. Exploring Antipsychotic Prescribing Behaviours for Nursing Home Residents with Dementia: A Qualitative Study

5.1 Chapter Description

In Chapter 4, I conducted a meta-ethnography and concluded that there were five key concepts influencing decision-making regarding antipsychotic prescribing in nursing home residents with dementia: *Organisational Capacity; Individual Professional Capability; Communication and Collaboration; Attitudes; Regulations and Guidelines.* Upon scrutinising these findings, it was evident that there were two important, interlinked target behaviours that required deeper investigation through further primary qualitative research (*appropriate requesting* and *appropriate prescribing* of antipsychotics by nurses and GPs respectively). In this chapter, I conduct semi-structured interviews based on the Theoretical Domains Framework (TDF), to explore the determinants of these target behaviours, with a view to informing a theoretically-informed, evidence-based, and sustainable behaviour change intervention.

The work of this chapter has been published as: *Walsh KA, Sinnott C, Fleming A, Mc Sharry J, Byrne S, Browne J, Timmons S. Exploring Antipsychotic Prescribing Behaviors for Nursing Home Residents With Dementia: A Qualitative Study. Journal of the American Medical Directors Association. In Press. 2018. (4)*

5.2 Abstract

5.2.1 Objectives:

Caution is advised when prescribing antipsychotics to people with dementia. This study explored the determinants of appropriate, evidence-based antipsychotic prescribing behaviours for nursing home residents with dementia, with a view to informing future quality improvement efforts and behaviour change interventions.

5.2.2 Design:

Semi-structured qualitative interviews based on the Theoretical Domains Framework (TDF).

5.2.3 Setting and Participants:

A purposive sample of 27 participants from four nursing homes, involved in the care of nursing home residents with dementia (eight nurses, five general practitioners, five healthcare assistants, three family members, two pharmacists, two consultant geriatricians and two consultant psychiatrists of old age) in a Southern region of Ireland.

5.2.4 Measures:

Using Framework Analysis, the predominant TDF domains and determinants influencing these behaviours were identified, and explanatory themes developed.

5.2.5 Results:

Nine predominant TDF domains were identified as influencing appropriate antipsychotic prescribing behaviours. Participants' effort to achieve *"a fine balance"* between the risks and benefits of antipsychotics was identified as the cross-cutting theme that underpinned many of the behavioural determinants. On one hand, neither healthcare workers nor family members wanted to see residents over-sedated and without a quality of life. Conversely, the reality of needing to protect staff, family members and residents from potentially dangerous behavioural symptoms, in a resource-poor environment, was emphasised. The implementation of best-practice guidelines was illustrated through three explanatory themes (*'human suffering'; 'the interface between resident and nursing home';* and *'power and knowledge: complex stakeholder dynamics'*) which conceptualise how different nursing homes strike this *"fine balance"*.

5.2.6 Conclusions:

Implementing evidence-based antipsychotic prescribing practices for nursing home residents with dementia remains a significant challenge. Greater policy and institutional support is required to help stakeholders strike that *"fine balance"* and ultimately make better prescribing decisions. This study has generated a deeper understanding of this complex issue and will inform the development of an evidence-based intervention.

5.3 Introduction

Guidelines advise against antipsychotics for the first-line management of BPSD (14, 59), due to the increased risks of stroke and mortality (109, 112, 114). However, antipsychotics can be appropriate when behavioural symptoms are severe, dangerous, or distressing to the person with dementia (14, 59). Despite the existence of guidelines for over a decade and national level efforts to improve dementia care, antipsychotic prescribing is still common, especially in nursing home settings (80, 147, 358). Global estimates of antipsychotic prescribing prevalence in nursing home residents vary from 16% in the US (139), 19% in England (147), to 27% across Western Europe (80).

A systematic review examining the effectiveness of interventions to reduce inappropriate prescribing of antipsychotics to nursing home residents with dementia, reported that the majority of interventions were effective in the short-term (151). However the long-term effects were assessed in only four studies, with prescribing returning to baseline levels in two studies (359, 360).

Successful implementation of evidence-based practice requires effective and sustained behaviour change, beginning with a thorough understanding of the problem (162). A body of qualitative research has explored problematic clinical decision-making in this area. As discussed in Chapter 4, we conducted a systematic review of this literature, and found that the use of antipsychotics in nursing homes is the culmination of a range of healthcare professional behaviours (3). The two main behaviours identified were appropriate requesting and prescribing of antipsychotics. However, there has been a lack of exploration of these behaviours as standalone

processes and in terms of how they influence each other. Furthermore, there has been limited exploration of how different stakeholders perceive these interacting behaviours. Hence gaps in our understanding remain, which will be best answered by further qualitative research.

The TDF is an integrative framework of influences on behaviour, identified by synthesising multiple behaviour change theories (361). The TDF consists of 14 domains (**Table 11**), and provides a comprehensive, theory-informed approach to identifying the determinants (i.e. barriers and facilitators) which influence clinical behaviours (361). Utilisation of the TDF will help us to identify the determinants which influence prescribing behaviours and hence support progression from exploration to intervention (362).

The aim of this qualitative study was to explore and interpret the determinants of appropriate prescribing behaviours (requesting and prescribing) among a range of individuals involved in the care of nursing home residents with dementia, with a view to informing future quality improvement efforts and behaviour change interventions.

Table 11: Theoretical Domains Framework (TDF) Definitions

Domain	Definition
Behavioural Regulation	Anything aimed at managing or changing objectively observed or measured actions
Beliefs about Capabilities	Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use
Beliefs about Consequences	Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation
Emotion	A complex reaction pattern, involving experiential, behavioral and physiological elements, by which the individual attempts to deal with a personally significant matter or event
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
Goals	Mental representations of outcomes or end states that an individual wants to achieve
Intentions	A conscious decision to perform a behaviour or a resolve to act in a certain way
Knowledge	An awareness of the existence of something
Memory, Attention and Decision-Processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives
Optimism	The confidence that things will happen for the best or that desired goals will be attained
Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus
Skills	An ability or proficiency acquired through practice
Social Influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours
Social/Professional Role and Identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting

5.4 Methods

5.4.1 Study Design

We conducted semi-structured interviews, based on the TDF, with a range of healthcare workers and family members involved in the care of nursing home residents with dementia, in Cork, Ireland. Ethics approval was granted by the local ethics committee (Appendix 12). The *'COnsolidated criteria for REporting Qualitative research'* (COREQ) statement guided study reporting (Appendix 5) (363). Two PPI advisory groups composed of four people with dementia in one group, and two family members in the other group, provided input into topic guide development and recruitment. Advisor eligibility criteria included being a person with dementia affiliated with the Alzheimer Society of Ireland or a family member of any nursing home resident with dementia, and having an interest in research aimed at improving the quality of medication usage in nursing homes. Written informed consent was obtained from all advisors.

5.4.2 Study Setting and Sampling

Nursing homes were chosen as the focus of this study as the prevalence of antipsychotic use is highest in these settings, as found in Chapter 3 (2, 364). Participants were purposively sampled, according to our sampling framework (**Table 12** below), to ensure a heterogeneous group with maximum variation according to two main pre-determined criteria (*Professional/social role* and *nursing home type*). We also used snowball sampling to fulfil our sampling framework requirements.

Six different nursing home sites were selected based on our sampling framework, through publicly available directories of registered nursing homes on the HIQA (134) and Nursing Home Ireland websites (365). The Directors (Nursing or Medical) of each nursing home were contacted about the study. Once access was agreed, the Director and other consenting participants connected to that nursing home were interviewed. The Directors approached family members initially before recommending that they were suitable to be contacted.

Eligibility criteria for healthcare workers included being a physician (GP, geriatrician or psychiatrist of old age), a nurse, a pharmacist or a HCA who was involved in the care of nursing home residents with dementia. Eligibility criteria for family members included being a relative of a nursing home resident with dementia (alive or deceased), who had been prescribed an antipsychotic for BPSD.

5.4.3 Data Collection

We developed separate topic guides for healthcare professionals, HCAs and family members (Appendix 6). Topic guides were iteratively developed using findings from our systematic review (3), the TDF, advisor recommendations and five pilot interviews. The topic guides underwent revisions throughout the study to ensure that emerging themes were captured in subsequent interviews. All interviews were conducted by the primary researcher. Written informed consent was obtained prior to interviews. All interviews were audio-recorded and transcribed verbatim. The author wrote detailed field notes immediately after interviews, to refine topic guides and inform data analysis. We sampled until no new ideas emerged and conducted three more interviews without any new ideas emerging to ensure that data

saturation had been reached (366). The interviews were conducted between July 2016 and April 2017.

There were no established relationships between any participants and the research team prior to study commencement. The primary author informed all participants prior to commencing interviews, that he was a pharmacist undertaking this study as part of his PhD, and for the purpose of the interview, he was asking questions as a researcher, and not as a pharmacist.

5.4.4 Data Analysis

Data analysis followed the principles of Framework Analysis (356) and utilised NVivo version 11 for data management purposes (304). We utilised both deductive and inductive approaches to analysis throughout the five stages of Framework Analysis (*familiarisation, identifying a thematic framework, indexing, charting,* and *mapping and interpretation*). First, the author became *familiar* with the data by reading transcripts and field notes and open coded across the entire dataset. During *indexing*, data from the transcripts were deductively coded into one or more TDF domains according to the definitions for each domain (**Table 11**). Simultaneously, concepts emerging from the open coding were categorised inductively. These simultaneous *indexing* steps were conducted independently by three authors (KW, AF, JMcS) for seven transcripts, who met to discuss differences in TDF application or interpretation of emerging concepts, and came to consensus. The *indexing* of the remaining transcripts was conducted by the primary author.

Charting of the data, with distilled summaries in matrix format was used to identify the predominant TDF domains influencing the target behaviours (appropriate

requesting and prescribing) (362). This was performed independently by two authors (KW and CS), who then discussed any disagreement until consensus was reached. From these predominant domains, the determinants (i.e. barriers and facilitators) of the target behaviours were identified.

For the *mapping and interpretation* step, we iteratively developed links between determinants, predominant domains, categories and theory to provide overall explanations for the findings. This was achieved by constructing conceptual mind maps exploring possible relationships between all these different factors. By iteratively examining these evolving conceptual mind maps as an interdisciplinary research group (consisting of pharmacists, a GP, a health psychologist, a methodologist and a geriatrician), we were able to condense our findings into three explanatory themes and one overarching theme. Therefore the behavioural determinants were the *'building blocks'* for the themes, and an overarching theme was identified, explaining the relationship between behavioural determinants and explanatory themes. These stages were not linear (**Figure 22**), and the data collection and analysis phases occurred concurrently, to enable the exploration of emergent themes in subsequent interviews and to identify when data saturation occurred (366).

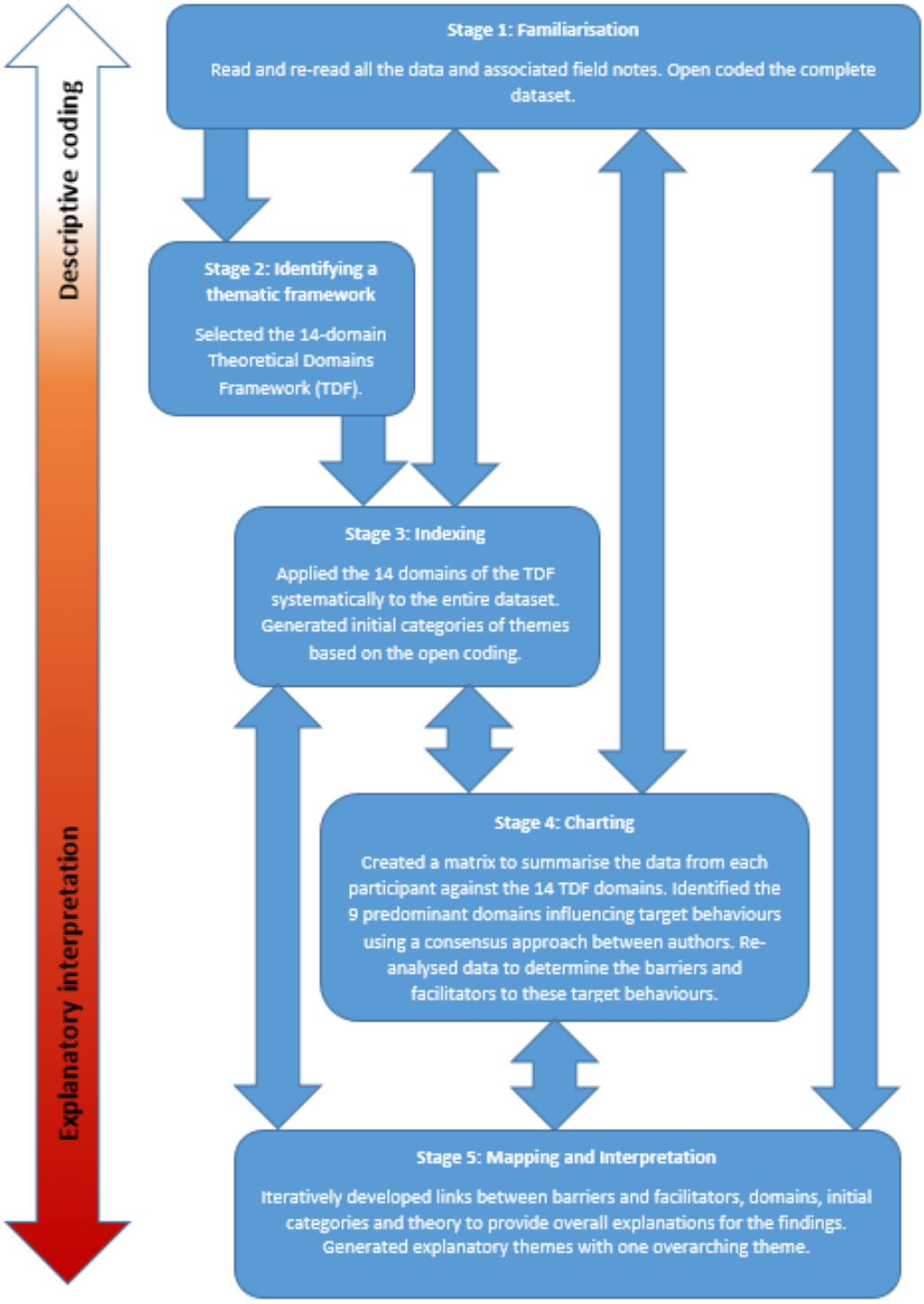

Figure 22: The five iterative stages of Framework Analysis

5.5 Results

We invited six nursing homes to participate and four agreed - two private nursing homes, one with and one without a dementia specialist care unit (SCU); one voluntary nursing home (state-funded but charitable organisation governance) without a SCU; and one public nursing home (state-run) without a SCU (**Table 12**). Of 38 individuals contacted, 27 agreed to participate (eight nurses, five GPs, five HCAs, three family members, two pharmacists, two consultant geriatricians and two consultant psychiatrists of old age) (**Table 12**). The median interview length was 23 minutes (range 12-56 minutes). The characteristics of the 27 interview participants are outlined in **Table 13**.

Table 12: Sampling Framework

	Nursing Home Type			
Professional/social Role	Private Nursing Home (n=2)	Voluntary Nursing Home (n=1)	Public Nursing Home (n=1)	Total
General Practitioner	2	1	2	5
Nurse	5	2	1	8
Pharmacist	1	1	0	2
Healthcare Assistant	2	2	1	5
Family member	3	0	0	3
Consultant Psychiatry of Old Age	2			2
Consultant Geriatrician	2			2
TOTAL				**27**

The number in each box refers to the number of participants recruited, according to the two main pre-determined criteria (Professional/social role and nursing home type).

Table 13: Characteristics of Interview Participants

Characteristics of total participants (n=27)	Participants, n
Professional/social role	
Nurse	8
General Practitioner	5
Healthcare Assistant	5
Family Member	3
Pharmacist	2
Consultant Geriatrician	2
Consultant Psychiatrist of Old Age	2
Gender	
Female	17
Male	10
Other	0
Category of Nursing Home participant worked in*	
Private only	9
Public only	4
Voluntary only	3
Multiple	8
Years of professional experience (since qualification)*	
<10 years	3
10-19 years	10
≥20 years	10
Information not provided	1
Received specialist dementia training*	
Yes	16
No	8
Presence of dementia specialist care unit (SCU) in any nursing home participant worked in*	
Yes	7
No	17
Characteristics of Family Member Participants (n=3)	**Participants, n**
Gender	
Female	2
Male	1
Other	0
Category of Nursing Home person with dementia resides/resided	
Private	3
Role	
Current carer	1
Former carer	2
Age of participant	
40-49	1
50-59	1
60-69	1
Relationship to person with dementia	
Son/daughter	2
Nephew/niece	1

** N/A for n=3 family members*

We identified nine predominant TDF domains, encompassing 38 behavioural determinants that influenced our target behaviours (**Table 14** below). Broadly speaking, these nine TDF domains were relevant across both requesting and prescribing behaviours. We also developed three explanatory themes and one over-arching theme, which are discussed below and illustrated in a conceptual model (**Figure 23**). The nine predominant TDF domains and the more seminal determinants are discussed below; detail on the remaining determinants is presented in **Table 14**. Professional differences were not the primary focus of this study, however if any differences were noticeable, we have reported on these below.

5.5.1 Predominant TDF domains

5.5.1.1 Behavioural Regulation

Participants believed that HIQA, the independent nursing home regulator in Ireland, has put antipsychotics under scrutiny. Regulation now requires nursing homes to notify HIQA, on a quarterly basis, of any occasion when restraint (chemical or physical) is used (137). Some participants believed that these regulations made them re-evaluate how they manage BPSD, with positive outcomes for residents.

> *"I think HIQA is brilliant... because I really think they force people to look at their practice, and to challenge their own practice and to change." [HCA 1]*

However, GPs in particular, felt that there was over-regulation by HIQA, resulting in increased administrative burden, which did not necessarily translate into good care.

Furthermore, some participants were confused by the regulatory requirements, and were concerned about unintended negative consequences, because of the mistaken belief that only psychotropic medications used for acute episodes were reportable.

> *"Now, conversely, what it has made some nursing homes do is, if somebody was on a PRN psychotropic, because the resident might only need it once or twice per month and because it becomes reportable, they get prescribed regularly." [Nurse 5]*

Healthcare workers reported that interdisciplinary medication reviews, audits and internal registries also provided an opportunity for self-monitoring. When in place, these systems assisted with the identification of patterns of inappropriate usage. Prescribers found international guidelines helpful in their decision-making (14). However, succinct guidelines specific to the Irish context were sought.

5.5.1.2 Beliefs about Capabilities

Participants struggled to find solutions to BPSD other than antipsychotics in part because they felt that they lacked necessary training. Nursing home staff struggled with the daily management of BPSD and some admitted that they needed antipsychotics to cope. GPs often felt out of their comfort zone and regularly needed input from specialists.

> *"In some ways I don't feel I have the sufficient expertise to make those decisions so I'll look to specialists at that point if I'm struggling with something." [GP 3]*

5.5.1.3 Beliefs about Consequences

Both healthcare workers and family members were worried about side effects such as sedation and falls. Some viewed these side effects as undignified and inhumane, and hence were reluctant to request or prescribe antipsychotics.

A fear of negative consequences (i.e. adverse behavioural events from residents) if antipsychotics were not prescribed was expressed by prescribers. They were conscious of the safety of their nursing home colleagues who were often at the receiving end of behaviours.

> *"Because you don't know what precipitated the [behaviour], and then, when you're trying to pull back and you walk away, are you leaving your colleagues in the height of it then?" [GP 4]*

5.5.1.4 Emotion

Participants, particularly family and nursing home staff, spoke emotively about BPSD, and how these symptoms deeply impacted upon them personally. Sometimes participants believed that antipsychotics were the only solution to alleviating this distress.

> *"It was very hard to listen to [the BPSD]… so as far as I'm concerned, if there was a medication that would sort this thing anyway, I certainly was completely open to it." [Family member 2]*

Nursing home staff were deeply affected by behaviours leading to burn-out, frustration and poor morale. Staff sometimes took behaviours personally, which could increase the propensity to request prescribing of antipsychotics. Empathy as opposed to sympathy was viewed as an important trait when dealing with BPSD. It

was seen to be important to be able to step back, evaluate the situation and determine the best course of action for the resident, without emotions clouding one's judgement.

> *"I feel that certain people take huge offence if a person who is cognitively impaired lashes out, punches, screams, whatever, and you have to let it go." [Nurse 8]*

5.5.1.5 Environmental Context and Resources

The overall picture was one of poor resources in nursing homes. Although non-pharmacological interventions were generally seen as the gold standard, there was consensus that these interventions were staff-intensive and not always feasible.

> *"You need to have the time to be with somebody, staffing levels don't really give you the opportunity to sit with somebody all day long or all afternoon… you can come and go but you can't stay with the person." [Nurse 4]*

The physical environment was believed to have a profound impact on residents. Some participants believed that if the environment was better suited to meet the needs of the resident, then there would be less of a need to prescribe.

> *"I think if we had properly designed purpose built modern dementia units that allowed us to offer a different environment than the standard ward environment… I do think that would be far more humane and you'll probably get better overall results than resorting to the old fashioned chemical restraints." [Consultant geriatrician 2]*

Participants described how treatment culture impacted on the resident in terms of prescribing, both positively (e.g. being resident-centred) and negatively (e.g. being task-orientated). There was a general agreement that every nursing home was completely different, and what may be acceptable in one nursing home may not be acceptable in another.

5.5.1.6 Knowledge

Both healthcare workers and family members were aware that antipsychotics cause side effects. However, non-consultants in particular, acknowledged their own limited knowledge on this topic, and welcomed further education. Furthermore, GPs believed that a better understanding of the risk/benefit profile among nursing home staff would reduce requests for antipsychotics.

> *"If you can tell someone what the potential complications [of antipsychotics] are, they may be a little bit less likely to ask for them." [GP 1]*

In-depth knowledge of the resident was believed to be paramount. Knowing the resident and understanding their life story helped nursing home staff to adapt the environment to meet the needs of the resident, and often prevented unnecessary prescribing.

> *"I think just knowing the person. Knowing that they have been on them [antipsychotics] for years. Looking at them now, their state of deterioration and you know in your heart and soul they don't need them." [Nurse 5]*

5.5.1.7 Memory, attention and decision-processes

The importance of conducting a holistic assessment of the resident was emphasised by participants. There was agreement that antipsychotics were only appropriate after all potential reversible causes of BPSD were ruled out. In one nursing home, where a comprehensive assessment protocol was recently introduced, nurses explained how this protocol assisted them with their decision-making.

5.5.1.8 Social Influences

Prescribers were based off-site so they relied on accurate and objective information about residents from nurses. Prescribers largely valued and trusted the nurses' judgements and tended to make prescribing decisions based on the information provided. However this could lead to a perception that behavioural symptoms were being exaggerated in order to increase the likelihood of prescription.

> *"I think people can be a little bit biased in how they can present a case to you at times to get to the ends that they want. I know there has been one incident where… a staff member [was overheard] saying 'sure just tell her she's had hallucinations.'" [GP 3]*

Prescribers reported that pressure to prescribe antipsychotics arose from many sources including individual staff members, family members, the nursing home organisation, and from society itself.

> *"So I feel under pressure to knock this person out, anaesthetise this patient, who they see as, shouldn't be challenging. And they're already completely over-sedated and the staff want them to be even more sedated." [Consultant psychiatrist of old age 2]*

There was a perception by some of a prevailing culture where all behaviours may be attributed to the disease rather than an unmet need. However, other participants felt that, due to the influence of HIQA, nursing homes were moving towards a more social model of care. This shift in culture was broadly welcomed. However, some physicians feared that the pendulum had "*swung too far" [Consultant psychiatrist of old age 1],* and that GPs, in particular, may be fearful of using antipsychotics due to the perceived anti-medication climate.

5.5.1.9 Social/Professional Role and Identity

Nursing home staff and family members viewed themselves as the resident's advocate. This role empowered them to speak up on behalf of the resident.

> *"See mom didn't have a voice, nobody would listen to her even when she was speaking, she wasn't listened to and I was her voice." [Family member 1]*

There was a hierarchy described by participants in the nursing home environment. HCAs were often not involved in any degree of decision-making despite their in-depth knowledge of residents. Furthermore, one pharmacist felt disregarded in this area, despite her pharmacological expertise. Decisions were perceived as being made between GPs and nurses, with input from consultants when needed.

> *"As it stands and we're talking about the real world, it's really the nursing staff and the GP. I don't have an influence there. If I get the script, we just have to hand it over." [Pharmacist 2]*

The importance of leadership from the nursing home manager was emphasised. Good leaders were perceived as those with experience who provided adequate training and support to staff.

Table 14: Determinants of appropriate antipsychotic prescribing behaviours

Determinants (i.e. barriers and/or facilitators) of appropriate antipsychotic prescribing behaviours (requesting and prescribing)	Illustrative quotes
1. Behavioral Regulation	
HIQA regulation as a stimulus for change **(facilitator)**	*I think HIQA is brilliant... because I really think they force people to look at their practice, and to challenge their own practice and to change." [HCA 1]*
Perception of HIQA over-regulation by GPs **(barrier)**	*"I think HIQA are a scurge. I wonder what they bring to the table. I think they're self-fulfilling... Ya I think most GPs would not [be happy with them]. I don't think they bring a whole lot to the table unfortunately. I think they bully private nursing home and private institutions…Ya I think it's all very, very good and ivory tower stuff and politically correct. But, could I think [sic] the money spent on HIQA could be spent better on direct services? Probably." [GP 1]*
Uncertainty regarding HIQA reporting requirements **(barrier)**	*"Now, conversely, what it has made some nursing homes do is, if somebody was on a PRN psychotropic, because the resident might only need it once or twice per month and because it becomes reportable, they get prescribed regularly." [Nurse 5]*
Self-monitoring (using local systems) of antipsychotic prescribing **(facilitator)**	*"So, for me it would be to monitor the scripts as they come in and maybe their charts and we do at the request of the Director of Care, we do a psychotropic audit every month. So we see where they're being reviewed." [Pharmacist 2]*
Guidelines for monitoring the appropriateness of antipsychotic prescribing **(facilitator)**	*"Guidelines is a good thing, and licensing, because you know there isn't any license. Grade one, grade two evidence, meta-analyses… You can certainly use them to say why you're not prescribing an antipsychotic. You just say there's no evidence and it's not national policy." [Consultant Psychiatrist of Old Age 2]*
2. Beliefs about capabilities	
Poor self-efficacy in the management of BPSD among non-specialists **(barrier)**	*"So I suppose in some ways I don't feel I have the sufficient expertise to make those kind of decisions so I'll look to specialists at that point if I'm struggling with something." [GP 3]*
Belief that assessing whether an antipsychotic prescription is 'appropriate' or not is challenging **(barrier)**	*"It's a difficult one to decipher. When it's appropriate and when it's not appropriate." [Nurse 6]*
Belief that deprescribing antipsychotics is difficult **(barrier)**	*"And it's very easy starting these things but the discontinuation of them not quite so clear cut." [Consultant Geriatrician 2]*
3. Beliefs about consequences	
Concerns about side-effects **(facilitator)**	*"She was just asleep looking, absolutely drugged out of her tree looking, sitting in a chair." [Family member 1]*
Belief that antipsychotics are highly effective **(barrier)**	*"I know the drugs can fix these things. Now not completely right. But I know that drugs can fix these things." [Family member 2]*

Belief that NPIs are not a feasible alternative **(barrier)**	*"But if you have somebody at 2 o clock in the morning that you're pacing the floor with until 6 o clock in the morning, where are your therapies then?" [HCA 2]*
Belief that the return of symptoms are caused by the reduction of antipsychotic dosage **(barrier)**	*"I think people often think, that if something doesn't work straight way or if there happens to be a coincidental problem as soon as you start to reduce it, suddenly there is this complete fear that this has caused it, they expect more immediate, they see the immediate things as being either absent or present so when you start a new drug if it hasn't worked straight away there is a bit of 'oh it's not working.'" [GP 3]*
Anticipated regret **(barrier)**	*"Because you don't know what precipitated the [behaviour], and then, when you're trying to pull back and you walk away, are you leaving your colleagues in the height of it then?" [GP 4]*
4. Emotion	
Fear of dementia **(barrier)**	*"It was very hard to listen to [the BPSD]… so as far as I'm concerned, if there was a medication that would sort this thing anyway, I certainly was completely open to it." [Family member 2]*
Taking behaviours personally **(barrier)**	*"I feel that certain people take huge offence if a person who is cognitively impaired lashes out, punches, screams, whatever and you know, you have to let it go." [Nurse 8]*
Burn-out and frustration **(barrier)**	*"You'll get staff who are burned out, they just can't cope. They're sick of saying X, Y and Z and they're not being listened to, and they just don't care anymore." [Nurse 3]*
Empathy toward people with dementia **(facilitator)**	*"I think people with a very empathetic view of dementia would be less likely to encourage, prescription of antipsychotics, because there is that, 'oh it's, you know, you don't have to give them drugs for it, it's just their dementia, we can get around it,' and then, some people… will see the more negative side of the dementia, and be like, 'isn't it awful for them, God wouldn't you just give them something to relax them.' [Nurse 6]*
Emotions of healthcare professionals tend to reflect those of family members **(barrier)**	*"I'll get [a phone call], 'The family were in today they're very worried about mammy. She's very upset and agitated'. I never get those phone calls to say that they're worried that's she's just sitting there staring into space." [GP 1]*
Personal experience of dementia **(barrier/facilitator)***	*"We're all human, we all bring our own stuff." [HCA 3]*
5. Environmental Context and Resources	
Lack of adequate resources **(barrier)**	*"You need to have the time to be with somebody, staffing levels don't really give you the opportunity to sit with somebody all day long or all afternoon… you can come and go but you can't stay with the person." [Nurse 4]*
Perception that it's cheaper to give antipsychotics than deliver NPIs **(barrier)**	*"They haven't enough staff and they seem to think that the cheapest way is to dose them, and keep them quiet" [Family member 1].*
Impact of the built environment on the person with dementia **(facilitator/ barrier)***	*"I think if we had properly designed purpose built modern dementia units that allowed us to offer a different environment than the standard ward environment… I do think that would be far more humane and you'll probably get better overall results than resorting to the old fashioned chemical restraints." [Consultant geriatrician 2]*
Each nursing home is different **(facilitator/barrier)***	*"You go to different nursing homes and attitudes are very different." [Nurse 3]*
Impact of treatment culture on residents **(facilitator/barrier*)**	*"Sometimes it can feel like the person is there as… I don't know how to say this politely, but they're in the bed and they have to acquiesce or be compliant with the system around them, be good children or good grown-ups and play the game. And if you don't do that, then you get labelled and your behaviour gets labelled." [Consultant Psychiatrist of Old Age 1]*
6. Knowledge	
Knowledge of antipsychotics **(facilitator)**	*"If you can tell someone what the potential complications [of antipsychotics] are, they may be a little bit less likely to ask for them." [GP 1]*
Knowledge on the cause and nature of BPSD **(facilitator)**	*"I think if people understood… why [residents] have behaviours that challenge I think that would go a long way for a lot more understanding and people not wanting just to sedate somebody." [Nurse 3]*
Knowledge of the resident **(facilitator)**	*"I think just knowing the person. Knowing that they have been on them [antipsychotics] for years. Looking at them now, their state of deterioration and you know in your heart and soul they don't need them." [Nurse 5]*

7. Memory, attention and decision-processes	
Decision-making based on a thorough assessment **(facilitator)**	*"Then with the physical as well, we do the PINCH ME acronym so we...pain, infection, constipation, hydration, nutrition, medications, environment, we look at real holistic view of the person and try and rule out any triggers there [sic]." [Nurse 6]*
Paying attention to *where* the challenge lies with regards to the behavioral symptoms **(facilitator)**	*"Sometimes it just ultimately again it takes me back, you need to take a step back, who are you treating? Are you treating the carer who wants a certain amount given so somebody is peaceful or a certain amount of investigation is done, or are we treating the staff who are treating the patient because they want a peaceful night or a peaceful day on the ward, or are we making a decision to make our own lives easier? And we just have to take a step back sometimes." [GP 5]*
8. Social Influences	
Social Pressure to prescribe **(barrier)**	*"So I feel under pressure to knock this person out, anaesthetise this patient, who they see as, shouldn't be challenging. And they're already completely over-sedated and the staff want them to be even more sedated." [Consultant psychiatrist of old Age 2]*
Reliance on accurate information from nursing home staff **(facilitator/barrier)***	*"I think people can be a little bit biased in how they can present a case to you at times to get to the ends that they want. I know there has been one incident where… a staff member [was overheard] saying 'sure just tell her she's had hallucinations.'" [GP 3]*
Modelling of prescribing behaviour **(facilitator/barrier)***	*"A lot of our learning seems to come from the consultations and referrals that we actually see what the psychiatry of the elderly prescribe in these situations, and we have been led by that, so quetiapine just seems to be one they seem to use." [GP 5]*
Prevailing culture of care **(facilitator/barrier)***	*"Medication comes first in Ireland. 'Give it to them as much as possible'". [Family member 1]*
9. Social/Professional Role and Identity	
Advocacy role of nursing home staff and family members **(facilitator)**	*"See mom didn't have a voice, nobody would listen to her even when she was speaking, she wasn't listened to and I was her voice." [Family member 1]*
Professional identity **(facilitator/barrier)***	*"It depends on what background you are coming from and when you trained, how you view the medications and the use of medications. I think there is a difference, between the younger generation of nurses and the older generation of nurses. There appears to be more of a reluctance, I think, in the younger generation of nurses with giving out, I suppose the high risk medications like [antipsychotics]… And I think there is a difference there then because you're not seeing your nursing profession as a medical profession, you're almost a facilitator...and when you see it from that perspective then medication isn't always the first kind of thing that pops into your head." [Nurse 6]*
Variable sense of responsibility for prescribing decisions **(facilitator/barrier)***	*"But I suppose it's up to the prescriber to be able to sort the wheat from the chaff and see what's a good grounded opinion and what's maybe not as reliable you know." [HCA 3]*
Leadership role of nursing home manager **(facilitator)**	*"You need a manager who is supporting staff and is knowledgeable and roles out good training to the staff. And has good experience so, and ideally good mental health experience because that's, not all of them have good mental health experience but it is important for the manager. If you meet the manager, you can usually see the tone of the home." [Consultant Psychiatrist of Old Age 2]*
Traditional hierarchy **(barrier)**	*"As it stands and we're talking about the real world, it's really the nursing staff and the GP. I don't have an influence there. If I get the script, we just have to hand it over." [Pharmacist 2]*

** This determinant could be a barrier or a facilitator depending on the individual circumstance*
BPSD: Behavioural and Psychological Symptoms of Dementia; GP: General Practitioner; HCA: Healthcare assistant; HIQA: Health Information and Quality Authority; NPIs: Non-pharmacological interventions; TDF: Theoretical Domains Framework

5.5.2 Explanatory themes

We identified *"a fine balance" [HCA 1]* as the over-arching theme. On one hand, neither healthcare workers nor family members wanted to see residents over-sedated and without a quality of life. Conversely, the reality of needing to protect staff, family members and residents from potentially dangerous behavioural symptoms, in a resource-poor environment, was emphasised. We found that nursing home staff and prescribers struggled with this constant tension throughout their daily practice.

Beneath the over-arching theme of *"a fine balance",* we developed three explanatory themes as a means of illustrating why this implementation issue, non-adherence to best-practice guidelines, persists. Within these themes, opposing perspectives and trade-offs were evident which can tip the *"fine balance"* in favour of undertaking one behaviour over another (e.g. prescribe versus not prescribe). We argue that the perspective of each nursing home towards these three explanatory themes, determines how they strike this *"fine balance"* (**Figure 23**).

5.5.2.1 Human Suffering

Participants described suffering related to both the disease and antipsychotic medications. Some viewed dementia as a terrible affliction: *"I think it's the hardest disease out there, to manage. It's one I would NOT like to get myself" [HCA 2].* Not only was dementia perceived to cause suffering to the resident, but often participants reported being physically and emotionally affected themselves. Antipsychotics were viewed through this perspective as a way of alleviating suffering for everyone. Conversely, others acknowledged that antipsychotics can cause severe

side effects for the resident, and were used primarily for *"staff-focused" [Consultant psychiatrist of old age 2]* as opposed to resident-focused purposes. From this perspective, the use of antipsychotics were frowned upon.

5.5.2.2 The Interface between Resident and Nursing Home

The perceived effect that the resident has on the nursing home, and vice versa, was the second explanatory theme. A resident exhibiting BPSD was perceived by some to have a negative impact on the nursing home environment, ultimately requiring additional staff and money: *"They haven't enough staff and they seem to think that the cheapest way is to dose them, and keep them quiet" [Family member 1].* From this perspective, antipsychotics were perceived as necessary to enable staff to care for all residents in an efficient manner. Conversely, the nursing home environment was perceived by others to have an important impact on the resident. From this perspective, placing the resident in *"the right place" [Nurse 3]*, i.e. a more dementia-friendly environment, was perceived to be more beneficial to the resident than any medication.

5.5.2.3 Power and Knowledge: Complex Stakeholder Dynamics

The final theme refers to the complex interplay between the many different stakeholders involved in the care of residents. The symbiotic concepts of power and knowledge can help us to understand these complex stakeholder dynamics. There were different types of knowledge valued by participants: knowledge of the disease, the drug and the resident. Often primacy was given to the latter. Hence from this perspective, nurses' in-depth knowledge of residents legitimised their power to request that an antipsychotic be started or stopped: "*The GP's will do it [deprescribe],*

no problem, we need to instigate it, and it's just the experience of knowing the person" [Nurse 5]. Conversely, others argued that those in higher positions of power had knowledge that was more important (i.e. knowledge of drug and disease), in determining the best outcomes for residents: *"Old age psych usually make a recommendation and then the GP will sign the prescription" [Nurse 8].* From this perspective, those in positions of power were perceived to have the most important knowledge in determining the appropriateness of antipsychotic prescribing.

Figure 23: Conceptual model of explanatory themes

Opposing perspectives and trade-offs (in white) can tip the "fine balance" in favour of undertaking one behaviour over another (e.g. prescribe versus not prescribe). The perspective of each nursing home toward these three explanatory themes (in blue), determines how they strike a "fine balance" between the risks and benefits of antipsychotics.

5.6 Discussion

Using a novel multi-perspective approach, we have generated a deeper understanding of the behavioural components of antipsychotic use in nursing home residents with dementia, the professional interactions that occur between different stakeholders and the determinants of implementation of best-practice guidelines. Our findings highlight how implementing evidence-based practice in this area remains a significant challenge, despite advances in knowledge and stricter regulations. We identified that stakeholders strive to strike *"a fine balance"* but ultimately, as humans, are influenced by interacting emotional, environmental, organisational and societal issues.

5.6.1 Comparison with Previous Research

This study builds on the findings of Chapter 4, where we identified five key concepts influencing decision-making: *organisational capacity; individual professional capacity; communication and collaboration; attitudes; and regulations and guidelines*. In this current study, we found all of these concepts also play a role in implementing evidence-based practice. With regards to *organisational capacity*, the fundamental issue of inadequate resources was discussed in almost all of our interviews. This current study also extends our understanding of the influence of *regulations* on practice. Our study confirms the important role of regulations, but also highlights unintended negative consequences that may occur as nursing homes undertake various workarounds. Similar workarounds have been reported in the US, where increasing diagnoses of schizophrenia in nursing home residents have been

observed, in a suspected attempt to exempt antipsychotics from regulatory reporting requirements (150). Almost 40% of US nursing home surveyors (who evaluate nursing home regulatory compliance through on-site inspections) have observed the creation of a new, but false diagnosis of psychosis in residents (367). Urick *et al.* surmise that the motive for falsification of records may be to improve a facility's *'five-star'* quality rating, as residents with schizophrenia and other select psychiatric conditions are exempt from the calculation of this quality metric (367)

We identified nine TDF domains that influenced our target behaviours, which are similar to those found in previous TDF studies exploring prescribing behaviours for various conditions (368-372). The key difference is our identification of *'emotion'* as a predominant domain which is absent in the majority of other prescribing studies (368-371). The emotional impact of BPSD on family members (49) and nursing home staff (373) is established in the literature. The concept that people with dementia inevitably lose their identity to dementia and thus become *'dehumanised'* has been hypothesised as a rationale for why family members often struggle with BPSD (49). In our study, this fear of dementia emerged as an important issue. It is evident that this impacts not only on family members, but also nursing home staff. Prescribers believe that sometimes it is challenging to decipher who precisely is distressed by the BPSD.

Foucault wrote that power and knowledge are not independent entities but are inextricably linked — *'knowledge is always an exercise of power and power always a function of knowledge'* (374). This theory may help us to understand the complex dynamics between hierarchical stakeholders and how different types of knowledge

are valued by different stakeholders. Knowledge of the resident tends to be prioritised, and sometimes this can contradict with treatment goals set by those in higher positions of power (with different types of knowledge). Hence, advocating on behalf of the resident, particularly by nurses, is central to decision-making, and a key target for potential intervention (375, 376).

Previous studies have explored the challenges GPs experience when managing BPSD (9, 354, 377). Jennings *et al.* identified three main challenges: lack of clinical guidance; stretched resources; and difficulties managing expectations (354). Our study corroborates these findings by highlighting the multitude of difficulties GPs face when deciding whether to prescribe antipsychotics or not. However, our study goes further by exploring the perspectives of a wider range of stakeholders, allowing us to gain a more holistic insight into this implementation problem.

5.6.2 Implications

It is evident that greater policy and institutional support is required to help stakeholders strike that *"fine balance"* and ultimately make better prescribing decisions. Development of national clinical guidelines may be one appropriate policy intervention. Such guidelines are currently being developed in Ireland as a priority action point of the national dementia strategy (378). An important implication of our study is the need to clarify existing regulations for stakeholders, as it is evident that they are unsure as to which prescribing scenarios are reportable and which are not, and residents may be adversely affected by this confusion.

Further consideration should also be given to the design of future nursing homes. Our findings highlight the importance stakeholders attribute to dementia SCUs in

terms of meeting the needs of residents with dementia. However, resident outcomes from SCUs have been mixed, along with concern over higher levels of antipsychotic usage (320, 379). Therefore, although SCUs may be desired by stakeholders, more evidence of the quality and safety of this approach is required before widespread adoption.

The perceived impact of treatment culture on antipsychotic usage featured heavily throughout this study. In line with previous systematic review findings (3, 380), the Nursing home manager was seen as a key determinant of nursing home treatment culture, as they possessed both a position of power and knowledge of the resident. We recommend that nursing home managers take advantage of their influential role by providing/organising ongoing training to staff as well as encouraging the involvement of peripheral stakeholders (i.e. HCAs, pharmacists, family members) in decision-making.

Despite guidance on avoiding antipsychotics in dementia, they can play an essential role in certain situations (14, 59). Our study shows that due to the stigma attached to antipsychotics, some prescribers are fearful of prescribing them at all, risking unnecessary distress for a resident for whom the medications are indicated. A recent study demonstrated that discontinuation of antipsychotics, without non-pharmacological substitution, can have a detrimental impact on residents' health-related quality of life (381). Our findings suggest that an evidence-based, standardised approach involving interdisciplinary collaboration, careful documentation and regular review is needed to ensure the most appropriate use of both pharmacological and non-pharmacological interventions (382). One such model

programme is the DICE (describe, investigate, create, and evaluate) approach, which promotes a holistic, person-centred approach to managing BPSD (32, 382).

Educational programmes are the most common intervention type utilised to tackle inappropriate antipsychotic prescribing (151) e.g. the OASIS programme (383), the HALT (Halting Antipsychotic use in Long-Term care) study (384) and the RedUSe (Reducing Use of Sedatives) project (359). Ongoing education and training to both nursing home staff and prescribers is an important aspect of ensuring appropriate antipsychotic prescribing, but is not sufficient on its own. Drawing from these existing programmes (359, 382-384) as well as our own findings, we recommend that future programmes should include training on the assessment and management of BPSD, dealing with emotions and managing expectations. It is important for prescribers to be empathetic and acknowledge the emotional and physical impact of BPSD, while assertively conveying, the limited benefit and serious risks associated with antipsychotics. Likewise, nurses as the key influencer on prescribing, should be aware of and communicate these issues to others within the nursing home and to family members. In particular, the OASIS communication training programme enforces these key messages (383). Consideration should also be given to the professional status of the person delivering the intervention, as it was evident that some healthcare professions were perceived as being more influential than others in terms of changing behaviour, in an Irish context (e.g. GP vs. pharmacist). Future research should focus on determining how best to deliver educational interventions, by whom, and alongside what, in order to achieve sustainable results.

5.6.3 Strengths and Limitations

The trustworthiness of our findings are underpinned by the involvement of different disciplines on our research team, our PPI advisory groups and the participation of multiple stakeholders from different organisations during the interviews. Triangulation of analysts and participants also contributed towards the credibility of the results. Interviews took place in one region in Ireland, but transferability is supported by the provision of sufficient contextual information to enable readers to determine how applicable our findings are to their own situation. Detailed reporting of well-established methods with diagrammatical audit-trails contributed towards the dependability of our findings. Finally, in terms of confirmability, detailed reporting of participants' quotations, helped ensure that our findings were primarily borne from the data (385).

Although 66% of nursing homes contacted and 71% of individuals contacted, agreed to participate in our study, it is possible that only those with strong views on this topic took part. Furthermore, although we employed a purposive sampling approach, Directors may have recommended individuals for participation who were more likely to provide favourable responses about practices in their nursing home. Hence the possibility of selection bias cannot be excluded. Random sampling of participants along with a larger sample may have reduced this problem, and may have allowed us to explore differences in perceptions between respondent groups and settings in greater detail (385).

Another limitation was the small number of family members recruited. The challenges of recruiting family members of residents with dementia to research

studies have been previously reported (386). Despite engaging with our advisors on this issue, and reminding Directors to identify potential participants, we only managed to recruit three family members. It is possible that family members were apprehensive about taking part due to the emotive nature of this topic. Furthermore, it is possible that the Directors may have been over-protective of family members.

5.7 Conclusions

Implementing evidence-based antipsychotic prescribing practices for nursing home residents with dementia remains a significant challenge, despite advances in knowledge and stricter regulations. In striving to strike *"a fine balance",* stakeholders are influenced by interacting emotional, environmental, organisational and societal issues. Greater policy and institutional support is required to help stakeholders strike that *"fine balance"* and ultimately make better prescribing decisions. This study provides us with a deeper understanding of this complex issue and will inform the development of a theory and evidence-based intervention.

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Walsh, K. 2019. Rationalising antipsychotic prescribing in dementia: a mixed-methods investigation. PhD Thesis, University College Cork.

Please note that Chapters 6, 7 & 8 (pp. 196-318) are unavailable due to a restriction requested by the author.

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Appendices

Appendix 1. Search Strategy for Chapter 2

Medline (OVID)

1.	Elderly.mp. OR “care of the elderly”.mp. OR “old age”.mp. OR “geriatric patients”.mp. OR exp Aged/ OR exp “Aged, 80 and over”/ OR exp Frail Elderly/ OR exp Age Factors/ OR exp Health Services for the Aged/ OR exp Geriatrics/ OR exp Aging/ OR exp Dementia/ OR exp Alzheimer Disease/
2.	“Medication appropriateness index”.mp. OR “screening tool of older persons prescriptions”.mp. OR “screening tool to alert doctors to right treatment”.mp. OR “assessing care of vulnerable elders”.mp. OR “potentially inappropriate prescribing”.mp. OR “potentially inappropriate medication”.mp. OR “inappropriate medication”.mp. OR “beers criteria”.mp. OR exp Inappropriate Prescribing/ OR “suboptimal prescribing” OR underprescribing.mp. OR overprescribing.mp.
3.	Exp Secondary Care/ OR exp Emergency Service, Hospital/ OR exp Patient Discharge/ OR exp Hospitalization/ OR exp Hospitals/ OR exp Patient Admission/ OR exp Academic Medical Centers/ OR exp Hospital Units/ OR exp Internal Medicine/ OR “hospital patient”.mp. OR hospitali*ed.mp. OR exp Inpatients/
4.	1 AND 2 AND 3

PubMed

1.	"geriatric nursing"[MeSH Terms] OR "pharmacies"[MeSH Terms] OR "pharmacists"[MeSH Terms] OR "professional role"[MeSH Terms] OR "physicians"[MeSH Terms] OR "patient care team"[MeSH Terms] OR "clinical pharmacy"[All Fields] OR "hospital pharmacist"[All Fields] OR "hospital pharmacy"[All Fields] OR "pharmacy"[MeSH Terms] OR pharmacist* [All Fields] OR "multi-disciplinary team"[All Fields] OR "medical specialist"[All Fields]
2.	"medication appropriateness index"[All Fields] OR "screening tool to alert doctors to right treatment"[All Fields]) OR "assessing care of vulnerable elders"[All Fields] OR "potentially inappropriate prescribing"[All Fields] OR "beers criteria"[All Fields] OR "suboptimal prescribing"[All Fields] OR underprescribing [All Fields] OR overprescribing[All Fields] OR "inappropriate prescribing"[MeSH Terms] OR "inappropriate medication"[All Fields] OR "potentially inappropriate medication"[All Fields]
3.	"pharmaceutical services"[MeSH Terms] OR "pharmaceutical care"[All Fields] OR "medical care"[All Fields] OR "screening"[All Fields] OR "drug monitoring"[MeSH Terms] OR "patient counseling"[All Fields] OR "patient counselling"[All Fields] OR "continuity of patient care"[MeSH Terms] OR "decision support techniques"[MeSH Terms] OR "evidence-based medicine"[MeSH Terms] OR "health promotion"[MeSH Terms] OR "practice guidelines as topic"[MeSH Terms] OR "self care"[MeSH Terms] OR "drug interactions"[MeSH Terms] OR "medication therapy management"[MeSH Terms] OR "integrated medicines management"[All Fields] OR "drug administration"[All Fields] OR "patient satisfaction"[MeSH Terms] OR "case management"[MeSH Terms] OR "drug therapy"[MeSH Terms] OR "drug utilisation review"[All Fields] OR "drug utilization review"[MeSH Terms] OR "pharmaceutical services"[MeSH Terms] OR "pharmacy service"[All Fields] OR "drug prescriptions"[MeSH Terms] OR "polypharmacy"[MeSH Terms] OR "medication errors"[MeSH Terms] OR "medication reconciliation"[MeSH Terms] OR "pharmaceutical preparations"[MeSH Terms] OR "quality assurance, health

	care"[MeSH Terms] OR "risk factors"[MeSH Terms] OR "geriatric assessment"[MeSH Terms] OR "health services misuse"[MeSH Terms] OR "drug utilisation"[All Fields] OR "drug utilization"[MeSH Terms] OR "drug-related side effects and adverse reactions"[All Fields] OR "interdisciplinary studies"[MeSH Terms] OR "interdisciplinary communication"[MeSH Terms] OR "clinical pharmacy information systems"[MeSH Terms] OR "decision support systems"[All Fields] OR "drug information services"[MeSH Terms] OR "physician's practice patterns"[MeSH Terms]
4.	**"aged"[MeSH Terms] OR "elderly"[All Fields] "age"[All Fields] OR "frail elderly"[MeSH Terms] OR "dementia"[MeSH Terms] OR "health services for the aged"[MeSH Terms] OR "geriatrics"[MeSH Terms] OR "old age"[All Fields] OR "elderly care"[All Fields] OR "geriatric patients"[All Fields] OR "geriatric disorder"[All Fields] OR "aging"[MeSH Terms] OR "age factors"[MeSH Terms]**
5.	**"secondary care"[MeSH Terms] OR "emergency service, hospital"[MeSH Terms] OR "patient discharge"[MeSH Terms] OR "hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitals"[MeSH Terms OR "patient admission"[MeSH Terms] OR "academic medical centers"[MeSH Terms] OR "hospital units"[MeSH Terms] OR "internal medicine"[MeSH Terms] OR "hospital patient"[All Fields] OR "patient readmission"[MeSH Terms] OR hospitalized[All Fields]) OR hospitalized [All Fields] OR "inpatients"[MeSH Terms]**
6.	**"intervention studies"[MeSH Terms] OR "clinical trials as topic"[MeSH Terms] OR "randomized controlled trials as topic"[MeSH Terms] OR ("research design"[MeSH Terms] OR "single-blind method"[All Fields] OR "follow-up studies"[All Fields] OR "prospective studies"[MeSH Terms] OR "health services research"[MeSH Terms] OR "random allocation"[MeSH Terms] OR "randomization"[All Fields] OR randomisation[All Fields] OR "control groups"[MeSH Terms]**
7.	**1 AND 2 AND 3 AND 4 AND 5 AND 6**

EMBASE

1.	**((('dementia'/exp or 'dementia') or ('alzheimers disease'/exp or 'alzheimers disease')) or (('aged'/exp or 'aged') or ('aging'/exp or 'aging') or ('geriatric disorder'/exp or 'geriatric disorder') or ('geriatric patient'/exp or 'geriatric patient') or ('elderly care'/exp or 'elderly care') or ('old age'/exp or 'old age') or ('elderly'/exp or 'elderly') or ('geriatrics'/exp or 'geriatrics') or ('frail elderly'/exp or 'frail elderly') or ('age factors'/exp or 'age factors')))**
2.	**(('internal medicine'/exp or 'internal medicine') or ('hospital admission'/exp or 'hospital admission') or ('hospital department'/exp or 'hospital department') or ('hospital discharge'/exp or 'hospital discharge') or ('hospital'/exp or 'hospital') or ('hospitalization'/exp or 'hospitalization') or ('hospital patient'/exp or 'hospital patient') or ('emergency ward'/exp or 'emergency ward') or ('university hospital'/exp or 'university hospital') or ('hospital readmission'/exp or 'hospital readmission') or ('hospital utilization'/exp or 'hospital utilization') or ('emergency care'/exp or 'emergency care') or ('ward'/exp or 'ward') or ('secondary care'/exp or 'secondary care') or hospitali*ed or inpatient*)**
3.	**(('controlled study'/exp or 'controlled study') or ('follow up'/exp or 'follow up') or ('intention to treat analysis'/exp or 'intention to treat analysis') or ('major clinical study'/exp or 'major clinical study') or ('randomized controlled trial'/exp or 'randomized controlled trial') or ('health services research'/exp or 'health services research') or ('control group'/exp or 'control group') or ('clinical trial'/exp or 'clinical trial') or ('evaluation study'/exp or 'evaluation study') or ('controlled clinical trial'/exp or 'controlled clinical trial') or ('intervention study'/exp or 'intervention study') or ('randomization'/exp or 'randomization') or ('prospective study'/exp or 'prospective study'))**

4.	**(('clinical pharmacy'/exp or 'clinical pharmacy') or ('physician'/exp or 'physician') or ('pharmacy'/exp or 'pharmacy') or ('pharmacist'/exp or 'pharmacist') or ('hospital pharmacy'/exp or 'hospital pharmacy') or ('medical specialist'/exp or 'medical specialist') or pharmacist* or ('pharmacies'/exp or pharmacies) or 'multidisciplinary team')**
5.	**(('inappropriate prescribing'/exp or 'inappropriate prescribing') or 'medication appropriateness index' or 'screening tool of older persons prescriptions' or 'screening tool to alert doctors to right treatment' or 'assessing care of vulnerable elders' or inappropriate next/1 medic* or overprescribing or underprescribing or 'beers criteria' or 'suboptimal prescribing')**
6.	**(('medical care'/exp or 'medical care') or ('pharmaceutical care'/exp or 'pharmaceutical care') or ('screening'/exp or 'screening') or ('drug therapy'/exp or 'drug therapy') or ('prevention'/exp or 'prevention') or ('prescription'/exp or 'prescription') or ('professional standard'/exp or 'professional standard') or ('interpersonal communication'/exp or 'interpersonal communication') or ('risk reduction'/exp or 'risk reduction') or ('risk factor'/exp or 'risk factor') or ('consultation'/exp or 'consultation') or ('health care utilization'/exp or 'health care utilization') or ('drug response'/exp or 'drug response') or ('drug use'/exp or 'drug use') or ('patient care'/exp or 'patient care') or ('drug'/exp or 'drug') or ('health care delivery'/exp or 'health care delivery') or ('health care facility'/exp or 'health care facility') or ('health care quality'/exp or 'health care quality') or ('health care utilization'/exp or 'health care utilization') or ('medical assessment'/exp or 'medical assessment') or ('medical information'/exp or 'medical information') or ('drug information'/exp or 'drug information') or 'lund integrated medicines management model' or ('health program'/exp or 'health program') or ('medication therapy management'/exp or 'medication therapy management') or ('patient counseling'/exp or 'patient counseling') or ('polypharmacy'/exp or 'polypharmacy') or ('evidence based medicine'/exp or 'evidence based medicine') or ('medication reconciliation'/exp or 'medication reconciliation') or ('health promotion'/exp or 'health promotion') or ('pharmaceutical services'/exp or 'pharmaceutical services') or ('pharmacy service'/exp or 'pharmacy service') or collaboration or ('team work'/exp or 'team work'))**
7.	**1 AND 2 AND 3 AND 4 AND 5 AND 6**

Centre for Reviews and Dissemination

1.	**(ward pharmacist) OR (geriatric nursing) OR MeSH DESCRIPTOR Geriatric Nursing EXPLODE ALL TREES OR (pharmacies) OR (pharmacists) OR (pharmacist) OR (pharmacy) OR (professional role) OR (physicians) OR (patient care team)**
2.	**(inappropriate prescribing) OR (potentially inappropriate prescribing) OR MeSH DESCRIPTOR Inappropriate Prescribing EXPLODE ALL TREES OR (medication appropriateness index) OR (beers criteria) OR (stopp/start) OR (stopp) OR (screening tool to alert doctors to right treatment) OR (screening tool of older persons prescriptions) OR (overprescribing) OR (underprescribing) OR (suboptimal prescribing) OR (acove) OR (assessing care of vulnerable elders) OR (inappropriate medication) OR (inappropriate medications) OR (inappropriate medication*) OR (priscus) OR (prescribing criteria) OR (screening tools for the elderly)**
3.	**1 AND 2**

Cochrane Database of Systematic Reviews

1.	**MeSH descriptor: [Geriatric Nursing] explode all trees, OR MeSH descriptor: [Pharmacies] explode all trees, OR MeSH descriptor: [Pharmacists] explode all trees, OR MeSH descriptor: [Professional Role] explode all trees OR MeSH descriptor: [Physicians] explode all trees OR MeSH descriptor: [Patient Care Team] explode all trees OR clinical pharmacy OR hospital pharmacy OR multidisciplinary OR interdisciplinary**
2.	**MeSH descriptor: [Inappropriate Prescribing] explode all trees OR inappropriate prescribing OR "medication appropriateness index" OR "screening tool to alert doctors to right treatment" OR "beers criteria" OR potentially inappropriate prescribing OR suboptimal prescribing OR over-prescribing OR under-prescribing**
3.	**MeSH descriptor: [Aged] explode all trees OR MeSH descriptor: [Aged, 80 and over] explode all trees OR MeSH descriptor: [Frail Elderly] explode all trees OR MeSH descriptor: [Health Services for the Aged] explode all trees OR MeSH descriptor: [Geriatrics] explode all trees OR old age OR old OR aging OR elderly OR MeSH descriptor: [Dementia] explode all trees OR MeSH descriptor: [Alzheimer Disease] explode all trees**
4.	**MeSH descriptor: [Patient Discharge] explode all trees OR MeSH descriptor: [Hospitals] explode all trees OR MeSH descriptor: [Patient Admission] explode all trees OR MeSH descriptor: [Academic Medical Centers] explode all trees OR MeSH descriptor: [Hospital Units] explode all trees OR MeSH descriptor: [Secondary Care] explode all trees OR secondary care OR hospitalization OR university hospital OR geriatric ward OR emergency department OR hospital OR secondary care setting**
5.	**1 AND 2 AND 3 AND 4**

CINAHL

1.	**alzheimer's disease OR dementia OR frail elderly OR geriatrics OR age factors OR aged, 80 and over aged OR old age OR health services for the aged OR care of the elderly OR elderly care OR "geriatric patient" OR "geriatric disorder" OR aging**
2.	**academic medical centers OR emergency department OR "care of the elderly ward" OR geriatric ward OR secondary health care OR "secondary care setting" OR secondary care OR patient admission OR hospitals OR patient discharge OR readmission OR inpatients OR hospitalization OR hospital units**
3.	**overprescribing OR underprescribing OR "suboptimal prescribing" OR "potentially inappropriate medication" OR "potentially inappropriate prescribing" OR "assessing care of vulnerable elders" OR "screening tool of older persons prescriptions" OR "screening tool to alert doctors to right treatment" OR beers criteria OR "medication appropriateness index" OR inappropriate prescribing**
4.	**1 AND 2 AND 3**

Web of Science

1.	**Inappropriate prescribing OR potentially inappropriate prescribing**
2.	**Patient discharge OR hospitalization OR hospitals OR patient admission OR academic medical centers OR hospital units**
3.	**Dementia OR alzheimers disease OR aged OR frail elderly OR age factors OR health services for the aged OR geriatrics**
4.	**Pharmacies OR pharmacists OR patient care team**
5.	**Prospective studies OR single-blind method OR follow-up studies OR health services research OR randomized**

6.	**1 AND 2 AND 3 AND 4 AND 5**

Science Direct

1.	**"clinical pharmacy" OR physician OR pharmacy OR pharmacist OR "hospital pharmacy" OR "medical specialist"**
2.	**"medical care" OR "pharmaceutical care" OR screening OR "drug therapy" OR prevention OR prescription OR "professional standard" OR "interpersonal communication" OR "risk reduction" OR "risk factor" OR consultation OR "health care utilization" OR "drug response" OR "drug use" OR "patient care" OR drug OR "health care delivery" OR "health care facility" OR "health care quality" OR "medical assessment" OR "medical information" OR "drug monitoring" OR "integrated medicines management" OR "health program" OR "medication therapy management" OR "patient counseling" OR polypharmacy OR "evidence based medicine"**
3.	**"inappropriate prescribing" OR "medication appropriateness index" OR "screening tool of older persons prescriptions" OR "screening tool to alert doctors to right treatment" OR "assessing care of vulnerable elders"**
4.	**aging OR "geriatric disorder" OR "geriatric patient" OR "elderly care" OR dementia OR "alzheimers disease"**
5.	**"internal medicine" OR "hospital admission" OR "hospital department" OR "hospital discharge" OR hospital OR "surgical ward" OR hospitalization OR "hospital patient" OR "emergency ward" OR "university hospital" OR "hospital readmission" OR "hospital utilization" OR "emergency care" OR ward**
6.	**"controlled study" OR "follow up" OR "intention to treat analysis" OR "major clinical study" OR "randomized controlled trial" OR "health services research" OR "control group" OR "clinical trial" OR "evaluation study" OR "controlled clinical trial" OR "intervention study" OR randomization OR "prospective study"**
7.	**1 AND 2 AND 3 AND 4 AND 5 AND 6**

ClinicalTrials.gov and metaRegister of Clinical Trials

“Medication appropriateness index” OR “beers criteria” OR “screening tool of older persons prescriptions” OR “screening tool to alert doctors to right treatment” OR “inappropriate prescribing” OR “potentially inappropriate prescribing”

ProQuest Dissertation and Theses

1.	**"prospective study" OR "randomized controlled trial" OR "randomised controlled trial" OR "single-blind" OR "follow-up studies" OR "cohort studies" OR "health services research" OR "controlled study" OR "intervention study"**
2.	**"patient discharge" OR hospitals OR "patient admission" OR "academic medical centers" OR "hospital units" OR "secondary care" OR hospitalization OR "university hospital" OR "geriatric ward" OR "emergency department" OR "secondary care setting"**
3.	**aged OR "frail elderly" OR "health services for the aged" OR geriatrics OR "old age" OR aging OR elderly OR dementia OR alzheimers disease**
4.	**"inappropriate prescribing" OR "potentially inappropriate prescribing" OR "medication appropriateness index" OR "screening tool to alert doctors to right treatment" OR "screening tool of older persons prescriptions" OR "beers criteria" OR "suboptimal prescribing"**
5.	**pharmacies OR pharmacist* OR "patient care team" OR "clinical pharmacy" OR "hospital pharmacy" OR multidisciplinary OR multidisciplinary OR interdisciplinary**
6.	**1 AND 2 AND 3 AND 4 AND 5**

Index to Theses in Great Britain and Ireland

“Inappropriate prescribing” OR “potentially inappropriate prescribing” OR stopp/start OR “beers criteria” OR “medication appropriateness index” OR “suboptimal prescribing”

Appendix 2. Search Strategy for Chapter 4

PubMed

1	"neuropsychiatric symptoms"[Title/Abstract] OR "neuropsychiatric symptom"[Title/Abstract] OR challenging behaviour[Title/Abstract] OR challenging behaviours[Title/Abstract]) OR "challenging behaviour"[Title/Abstract] OR "challenging behavior"[Title/Abstract] OR challenging behavior*[Title/Abstract] OR "behavioural and psychological symptoms of dementia"[Title/Abstract] OR "behavioral and psychological symptoms of dementia"[Title/Abstract] OR alzheimer*[Title/Abstract] OR "bpsd"[Title/Abstract] OR "alzheimer disease"[MeSH Terms] OR alzheimer disease[Title/Abstract] OR "dementia"[MeSH Terms] OR dementia[Title/Abstract]
2	"prescriptions"[MeSH Terms] OR prescriptions[Title/Abstract] OR deprescribing[Title/Abstract] OR "inappropriate prescribing"[MeSH Terms] OR inappropriate prescribing[Title/Abstract] OR prescrib*[Title/Abstract]
3	"antipsychotic agents"[MeSH Terms] OR "chemical restraint"[Title/Abstract] OR "pharmacological intervention"[Title/Abstract] OR antipsychotic agents[Title/Abstract]) OR neuroleptic*[Title/Abstract] OR "psychotropic drugs"[MeSH Terms] OR psychotropic drugs[Title/Abstract] OR psychotropic*[Title/Abstract]) OR anti psychotic*[Title/Abstract]
4	1 AND 2 AND 3

EMBASE

1	'dementia'/mj OR 'alzheimer disease'/mj OR bpsd:ab,ti OR 'behavioural and psychological symptoms of dementia':ab,ti OR 'behavioral and psychological symptoms of dementia':ab,ti OR (challen* NEXT/1 behav*):ab,ti OR alzheimer*:ab,ti OR 'neuropsychiatric symptoms':ab,ti OR 'neuropsychiatric symptom':ab,ti OR dementia:ab,ti
2	'neuroleptic agent'/mj OR 'psychotropic agent'/mj OR antipsychotic*:ab,ti OR neuroleptic*:ab,ti OR psychotropic*:ab,ti OR 'chemical cosh':ab,ti OR 'tranquilizer'/mj OR 'pharmacological intervention':ab,ti OR 'chemical restraint':ab,ti
3	'prescription'/mj OR 'inappropriate prescribing'/mj OR prescrib*:ab,ti OR deprescribing:ab,ti
4	1 AND 2 AND 3

MEDLINE (through OVID)

1	exp Dementia/ OR exp Alzheimer Disease/ OR dementia.ti,ab. OR alzheimer*.ti,ab. OR BPSD.ti,ab. OR "behavioural and psychological symptoms of dementia".ti,ab. OR "behavioral and psychological symptoms of dementia".ti,ab. OR (challeng* adj1 behav*).ti,ab. OR "neuropsychiatric symptoms".ti,ab. OR "neuropsychiatric symptom".ti,ab.
2	exp Antipsychotic Agents/ OR exp Psychotropic Drugs/ OR antipsychotic*.ti,ab. OR psychotropic*.ti,ab. OR neuroleptic*.ti,ab. OR anti-psychotic*.ti,ab. OR "pharmacological intervention".ti,ab. OR "chemical restraint".ti,ab. OR "chemical cosh".ti,ab.
3	exp Drug Prescriptions/ OR exp Inappropriate Prescribing/ OR prescrib*.ti,ab. OR deprescribing.ti,ab.
4	1 AND 2 AND 3

Academic Search Complete/CINAHL Plus/PsycINFO (EBSCO)

1	SU dementia OR TI dementia OR AB dementia OR SU alzheimer disease OR TI alzheimer disease OR AB alzheimer disease OR SU alzheimer* OR TI alzheimer* OR AB alzheimer* OR SU bpsd OR TI bpsd OR AB bpsd OR SU (challeng* N1 behav*) OR TI (challeng* N1 behav*) OR AB (challeng* N1 behav*) OR SU ("behavioural and psychological symptoms of dementia") OR TI ("behavioural and psychological symptoms of dementia") OR AB ("behavioural and psychological symptoms of dementia") OR SU ("behavioral and psychological symptoms of dementia") OR TI ("behavioral and psychological symptoms of dementia") OR AB ("behavioral and psychological symptoms of dementia") OR SU "neuropsychiatric symptoms" OR TI "neuropsychiatric symptoms" OR AB "neuropsychiatric symptoms" OR SU "neuropsychiatric symptom" OR TI "neuropsychiatric symptom" OR AB "neuropsychiatric symptom"
2	SU ANTIPSYCHOTIC AGENTS OR TI ANTIPSYCHOTIC AGENTS OR AB ANTIPSYCHOTIC AGENTS OR SU antipsychotic* OR TI antipsychotic* OR AB antipsychotic* OR SU psychotropic drugs OR TI psychotropic drugs OR AB psychotropic drugs OR SU psychotropic* OR TI psychotropic* OR AB psychotropic* OR SU neuroleptic* OR TI neuroleptic* OR AB neuroleptic* OR SU anti-psychotic* OR TI anti-psychotic* OR AB anti-psychotic* OR SU "pharmacological intervention" OR TI "pharmacological intervention" OR AB "pharmacological intervention" OR SU "chemical restraint" OR TI "chemical restraint" OR AB "chemical restraint" OR SU "chemical cosh" OR TI "chemical cosh" OR AB "chemical cosh"
3	SU prescribing OR TI prescribing OR AB prescribing OR SU inappropriate prescribing OR TI inappropriate prescribing OR AB inappropriate prescribing OR SU prescrib* OR TI prescrib* OR AB prescrib* OR SU deprescribing OR TI deprescribing OR AB deprescribing
4	1 AND 2 AND 3

Google Scholar Search Strategy

1	**Dementia**
2	**Antipsychotic**
3	**Prescribing**
4	**"Qualitative Research"**
5	**1 AND 2 AND 3 AND 4**

Journals Hand Searched and Alzheimer's Societies Contacted

Journals (Nov 2015 – July 2016)	International Alzheimer's Societies (contacted March 2016)
International Psychogeriatrics	Alzheimer's Society of Ireland
International Journal of Geriatric Psychiatry	Alzheimer Society UK
Age and Aging	Alzheimer Disease International
Dementia: International Journal of social research and practice	Alzheimer's Association
Alzheimer's and Dementia: The Journal of the Alzheimer's Association	Alzheimer Society of Canada
Alzheimer's and Dementia: translational research and clinical interventions	Alzheimer's New Zealand
Aging and mental health	Alzheimer's Australia
Journal of the American Medical Directors Association	
Journal of clinical nursing	
Journal of the American Geriatrics Society	
Drugs and Aging	
British Journal of Psychiatry	
Social Science and Medicine	
Implementation Science	
BMJ open	
American Journal of Alzheimer's & Other Dementias	
Research in Social and Administrative Pharmacy	

Appendix 3. ENTREQ Statement for Chapter 4

Item	Guide and description
1. Aim	To synthesize the findings from individual qualitative studies in order to develop novel interpretations of the influences on decision-making regarding the prescribing of antipsychotics in nursing home residents with dementia, with a view to informing intervention development and quality improvement in this field.
2. Synthesis methodology	Meta-ethnography as described by Noblit & Hare. This systematic interpretive approach was chosen as it is particularly useful for generating new theories or concepts, which can ultimately influence policy and practice
3. Approach to searching	Pre-planned, comprehensive search strategy to seek all available studies in the published literature according to a pre-planned, online PROSERO protocol (protocol registration CRD42015029141)
4. Inclusion criteria	Phenomenon of Interest: Antipsychotic prescribing in nursing home residents with dementia for the purpose of managing BPSD Population: Any person (healthcare professional, carer, patient) discussing the phenomenon of interest Language: English-language only Year: No exclusion based on year of publication Types of studies: Primary studies using qualitative research methods of data collection and data analysis, including mixed-methods studies. Articles published in full in peer-reviewed journals
5. Data sources	Electronic Databases: Medline (through OVID), PubMed, EMBASE, CINAHL, PsycINFO and Academic Search Complete. Supplementary methods: Hand-searching key journals and conference proceedings, citation searching of highly cited key papers, scanning reference lists of key papers and by contacting authors of relevant conference abstracts. Grey literature search: Google Scholar and by consulting the websites and key personnel from the various international Alzheimer's Societies (Appendix 2) Last search July 2018. An exhaustive search of the literature was conducted.
6. Electronic search strategy	Search strategy is described in detail in Appendix 2
7. Study screening methods	For the first stage of study selection, one reviewer (KW) conducted a preliminary screening of titles to exclude citations that were clearly not relevant (e.g. pre-clinical studies, systematic reviews). For the second stage, two reviewers (KW & RD) independently screened titles and abstracts, against inclusion criteria, to identify potentially relevant papers. In the third stage, two reviewers (KW & RD) independently reviewed the full texts of papers. Consensus on inclusion in stages two and three was reached by discussion between reviewers, with arbitration by a senior supervisor if required
8. Study characteristics	Details of the study characteristics are provided in Chapter 4.
9. Study selection results	Chapter 4 outlines the study selection process in a PRISMA flow diagram.
10. Rationale for appraisal	The purpose of quality appraisal was to assess the quality of study conduct.
11. Appraisal items	The CASP tool was used to appraise the included studies

12. Appraisal process	The quality assessment was conducted independently by two reviewers (KW & JB) and consensus reached by discussion.
13. Appraisal results	Study quality assessments are available in Chapter 4. We did not exclude studies on the basis of quality, as we believed all studies may still contribute some important insights to our phenomenon of interest. Critical weaknesses in study conduct were captured in the CERQual assessments and may have lessened confidence in certain review findings (Chapter 4).
14. Data extraction	All content in the results, discussion and conclusion sections of included papers were considered as data for analysis. These data were extracted onto a standardised word document by two reviewers independently, any discrepancies were resolved by discussion and then the data were uploaded onto a computer software programme. Information regarding: date of publication, country of conduct, setting, study objectives, participants, methodology, method of data collection and data analysis were extracted from the included studies and is presented in Chapter 4 to provide contextual information.
15. Software	NVivo version 11
16. Number of reviewers	Four reviewers were involved in reading all included studies in detail and constructing the initial key concepts (KW, RD, EC & CS). All 8 reviewers were involved in the translation and synthesis steps.
17. Coding	Comprehensive, line by line coding to search for concepts
18. Study comparison	In line with the constant comparative method of qualitative analysis the data were compared and contrasted across primary studies, to identify similarities and disagreements. Overarching concepts that represented the entire dataset were formulated after initial readings of the included papers. The specific contribution of each paper to each key concept was then determined (Appendix 4)
19. Derivation of themes	The process of developing the key concepts and sub-themes was inductive and iterative, moving from specific observations to broader generalizations or theories.
20. Quotations	Direct quotes from participants, and the interpretations of the authors of the primary studies are presented in the results section of the manuscript and in more detail in Appendix 4.
21. Synthesis output	Novel third-order interpretations were synthesized, which were subsequently linked together to develop a 'line of argument' representing the influences on decision-making regarding the prescribing of antipsychotics to nursing home residents with dementia. A conceptual model which illustrates this line of argument is presented in Chapter 4.

CASP, The' Critical Appraisal Skills Programme assessment tool for qualitative research'; CERQual, 'Confidence in Evidence from Reviews of Qualitative Research'; PRISMA, 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses'; ENTREQ, Enhancing the transparency in reporting the synthesis of qualitative research

Appendix 4. Translation between Included Studies for Chapter 4

Author (year)	Organisational Capacity		Individual Professional Capability		Communication & Collaboration		Attitudes towards people with dementia and the management of BPSD		Regulations and Guidelines
Sub-themes	Resources and access to services	Coping with the Severity of Behaviours	Skills	Knowledge	Communication within the healthcare team and with the family	Clarity of Roles & Responsibilities	Personal Attitudes	Organizational & Societal Attitudes	
Foley (2003)	-	*"His misbehaviours are so terrible. He has it in him to kill somebody; it's scary. I don't think he'd mean to, he just doesn't understand. He gets mad enough. I've caught him choking another resident in our dining room area, where the little quiet ladies sit, he was choking one of those little ladies. It's happened a number of times." (NH Staff member) (Page 111)* A sense of 'helplessness' develops among staff when severe behaviours are unpredictable and severe, when the resident has a true or suspected psychiatric comorbidity, and/ or when the size and	Physical aggression is the most difficult behaviour to manage, yet SCU [Specialist Care Unit] staff members in this study reported that they were equipped to manage *most* physically aggressive residents through behavioral and pharmacological interventions. This may be because of the observation that many aggressive behaviours are precipitated by some external event and are therefore predictable. (Page 120)	*"We actually had more family history on him [the successful resident], even though his wife was not here a lot, plus he had hobbies and things that we could zero in on. On the other hand, the other resident was a bachelor and lived by himself; the family didn't know him well. . . . That might have had some bearing on our success." (NH Staff member) (Page 119)* Many staff interviewees commented that the background information helped identify behavioral intervention strategies for difficult residents. (Page 118)	*"Always, at any point in time, there was support from the family… They gave us a lot of background information on this particular resident, and that's so very important... He [the husband] is there daily and is very supportive. It's nice to see that he can see her through the dementia." (NH Staff member) (Page 118)* Staff respondents reported that families often stayed involved through visits with the resident and communication with the staff, and that family support was critical to successful behaviour	-	*"…When he gets really bad, I just wish we had a padded room we could lock him in and let him go." (NH Staff member) (Page 116)*	*"'We learned not to force her into doing things, but to let her decide when she was ready. For example, just because everybody else ate at 7:00 didn't mean that she had to get up and eat then." (NH Staff member) (Page 114)*	-

		stamina of the resident interferes with management. (Page 122)			management. (Page 121)				
Patterson (2007)	*''So you know a specialist, somebody coming in there and looking at all the medication you know who knows medication, the pharmacology inside out, outside in, that's their job [a pharmacist], that's bound to be a bonus and it definitely will improve care.'' (Nursing Home Manager) (Page 520)* Greater involvement of pharmacists was supported by all participants. (Page 520)	-	-	*''Cause you know the resident, you're working with them, you see the changes, you know." (Nursing Home Manager) (Page 523)* The majority of nurse participants agreed that nurses were well placed to assess a resident's pharmaceutical care needs. (Page 523)	*''I think it's important to go back to the prescriber and say 'look do you realise that this is inappropriate?''' (Nursing Home Manager) (Page 522)* Participants also recognised the need to involve the prescribing GP in the pharmaceutical care process and this will require the establishment of pragmatic lines of communication. (Page 523)	*''I still have this bugbear of secondary prescribing being enforced on me, you know, I would have thought a consultant geriatrician would've sort of drastically cut drugs, you know, but whenever we get discharge from physicians or more you still find there are 6, 7, 8, 9, 10 drugs.'' (GP) (Page 521)*	*''They [antipsychotics] are definitely overprescribed especially for behavioural aspects''' (Older Person Advocate) (Page 520)* Many participants raised concerns over the use of these [antipsychotic] drugs, particularly with regard to their potential to cause adverse reactions with serious consequences for the elderly e.g. over-sedation and falls. (Page 520)	*''Doctors have said to me-'look I don't really want to prescribe temazepam, but they [nursing staff] want it and it's very difficult to refuse so 9 times out of 10 they would be prescribing it.''' (Prescribing Support Pharmacist) (Page 520)* All prescribing support pharmacist focus group participants referred to the overuse of psychoactive drugs suggesting that these drugs were prescribed for the convenience of nursing staff, which was also reported by the GPs. (Page 520)	-
Wood-Mitchell (2008)	*"If you go to do some work with proper challenging behaviour then it's a lot of man power- sort of*	*"I think that at all levels homes are dealing with a greater level of illness and disturbance than they were designed for."*	*"Yeah, the difficulty is, you know, there are good homes and bad homes, and often staff, both in terms of numbers of staff and their*	*"I think it's actually more of a problem of application of evidence actually. I think most of my colleagues would be aware of the*	*"Umm, and I would personally say [to a colleague], ''What [psychotropic] do you use? Do you use this a lot? Any problems you've*	"*It's actually quite difficult sometimes to say to staff 'well I'm not gonna give you any medication' cos*	*"I think there's a tendency to just to say well if someone has a dementia then the symptoms they're presenting with are just down to BPSD, it's*	*"Depending on which home you go to, there's probably a bit of pressure to do something." (Psychiatrist) (Page 549)*	*"There are times when I do go against the guidelines and do prescribe [Haloperidol]. But when there's been evidence of clear*

	observation, managing, coming back and checking, education for the staff and in some ways when resources are limited it's actually cheaper to just get me in, prescribe some medication for somebody." (Psychiatrist) (Page 549) A number of participants thought that the development of non-pharmacological treatments was being impeded, because using the medical model was seen as potentially a 'quick-fix' and a cheaper option. (Page 548)	*(Psychiatrist) (Page 549)* They [psychiatrists] believed that in order to reduce prescribing for this group, issues had to be addressed, particularly the nature and culture of care settings... (Page 551)	*quality, are very poor." (Psychiatrist) (Page 549)* The nature of care settings was viewed as important, with participants feeling that challenging behaviours were often the result of … inadequate staff training… (Page 548)	*limitations of the evidence of efficacy [of antipsychotics]." (Psychiatrist) (Page 550)* In general, participants often felt powerless to implement the findings from research, particularly in circumstances where they believed there was no alternative [to antipsychotics] to offer. (Page 551)	*found with it." (Psychiatrist) (Page 550)* Participants often liaised with colleagues and other professionals about which [psychotropic] medications to use, asking for advice on drugs and dosages. (Page 551)	*generally speaking that's what people are expecting." (Psychiatrist) (Page 549)*	*a homogenous condition, where I've never believed that is the case. It almost seduces you to practice rather sloppy psychiatry." (Psychiatrist) (Page 549)* A number of participants had an issue with regard to the concept of BPSD, believing it to be too broad. Owing to the use of such a poorly defined term, the psychiatrists believed that many 'unusual' behaviours could potentially be labelled as BPSD, thus meaning people missed the real cause of the behaviour (e.g. pain). (Page 548)	All participants felt strongly that there was pressure to prescribe. They considered this pressure was evident across settings, though varied in intensity. Psychiatrists thought the pressure from staff to prescribe was greatest in private-care settings.... (Page 550)	*benefit for the patient." (Psychiatrist) (Page 550)* What was more influential was past experience of a drug, although guidelines such as (Crosswalk Student Ministry) CSM were taken into account. (Page 551)
Kolanowski (2009)	*"…Getting the interventions out there even in the middle of the night or on the weekends." (NH staff member) (Page 216)*	*"They don't keep residents in the hospital a long time. So you know you're dealing with a lot of medical things. That unfortunately has to be our priority and the poor resident that's*	*"I don't think that new CNAs [certified nursing assistants] come out of class knowing how to deal with combative, aggressive, or apathetic*	*"We're learning new stuff all the time from the way that nursing homes used to be in the early 80's and how we treated residents with dementia. I mean they were all*	Interdisciplinary approaches to BPSD are quite effective, but there was scant evidence that these care providers were functioning as a unified team. (Page 219)	Findings indicate that staff maintains disciplinary ownership of interventions. Nurses and CNAs are at the bedside around the clock;	*"Just a little touch of something (medication) is helping her get to activities, not crying, not upset all evening and night you know ... So I don't think no pharmacology*	*"We don't tie them down. We find other ways." (NH Staff member) (Page 216)* Despite the emphasis on individualized care and culture change,	*"The first time I took [the restraint off] the resident fell and broke their hip. Again that was in '89 with OBRA when we first started, but I had to learn to take safety off the top of my list and put*

	Staffing patterns contribute to overuse of pharmacological interventions. Participants noted that it is often on evenings and weekends that medications are first ordered for the BPSD because there is insufficient staff at these times to do the needed one-on-one interventions. (Page 216)	*here with dementia is sort of left behind."(NH Staff member) (Page 216)* The rise in resident acuity level necessitates a careful balance of chronic and acute care in the same environment, and impacts the amount of time staff is able to spend with long-term residents. (Page 216)	*residents… they don't seek to understand the behaviour; they just try to address it and I think that's when you come up on failure because you don't really understand what's causing that behaviour." (NH Staff member) (Page 218)* Participants acknowledged they were poorly equipped to anticipate resident emotions and to deal with BPSD. A majority emphasized that a lack of "education in terms of dealing with persons with behavioral management dementia" created a barrier to understanding BPSD and applying non-pharmacological interventions. (Page 218)	*restrained chemically, physically." (NH Staff Member) (Page 216)* Staff understands that physical and chemical restraints are now regulated and that nursing homes need to provide individualized care when responding to BPSD. (Page 216)		their medical and recreational therapy colleagues are not. (Page 219)	*whatsoever is the answer." (NH Staff member) (Page 218)* The findings of this study confirm the nursing home staff's perceptions of pharmacological intervention as an efficient and reliable intervention to control behaviours in order to promote a calm environment for others. (Page 219)	for many staff the goal of care hasn't changed; control of behaviour is still a priority. Page 216)	*quality of life up there and put safety down here further." (NH Staff member) (Page 216)* Regulations and expectations around culture change are driving forces in the nursing home, setting the standard for quality of care. (Page 216)
Molinari (2011)	…A lack of available geriatric mental health professionals to adequately	-	The need for continued mental health training of staff… render[s] psychopharmacolog	Focus group data suggest that the NH staff are reasonably knowledgeable about how to	*"Teamwork is key". (NH Staff member*) (Page 908)	*"We often get dementia patients doped up from the hospital. It's convenient for*	Medications were viewed as a last resort by some; others suggested that in crisis	-	Cost-efficient quality assurance mechanisms must be developed and a variety of valid non-

	assess, diagnose, and treat mental health problems, … render[s] psychopharmacological care as the primary way of attempting to resolve a NH resident's distress. (Page 910)		ical care as the primary way of attempting to resolve a NH resident's distress. (Page 910)	address the mental health problems of residents (e.g. to individualize treatment, be flexible, don't use psychopharmacology as a first resort). (Page 909)	[Future] training should include modules on how to improve staff communication and teamwork on all staffing levels. (Page 910)	*them". (NH Staff member) (Page 908)* There was at least one comment in almost all of the groups regarding the perception that some of the NH residents were admitted on too much psychiatric medication and that it was their job 'to clean up the situation'. (Page 908)	situations one has to be flexible. (Page 908)		psychopharmacological evidence-based mental health programs be made available to assure that the spirit and intent of OBRA is realized. (Page 910)
Duxbury (2013)	Participants pinpointed factors that were important to successful aggression management, including… consistency of staffing, allowing staff to get to know residents well. (Page 799)	-	*"[You need to know] when to back-off a little bit from somebody who's aggressive, not argue, because I have seen people, they'll labour a point with a resident..." (Dementia Care Unit Manager) (Page 797)* Both staff and relatives recognized that they themselves could trigger aggressive behaviour through approaching people with dementia in	*"Staff really put 100% in here and they have their own individual patients who they know well." (Family Carer) (Page 797)*	*"We said if you hold her [down] we're happy, you know, it was awful; it really was awful." (Family Carer) (Page 798)* It was evident that relatives had some involvement in decisions regarding restraining residents. (Page 799)	-	*"I don't think it should just be prescribed as a matter of course really but I think with careful handling there is a role for it. I think if you have asked me that before she went in and before I knew what I know now, I would have said definitely not." (Family Carer) (Page 798)* It was accepted… that controlling strategies might need to be used in some circumstances. (Page 799)	*"I've been in homes where they've been I would say drugged up. You know they have a policy [here] that that doesn't happen and I admire them for that because they like the person to be the person." (Family Carer) (Page 798)* Both staff and relatives felt that controlling strategies (medication and restraint) should be used sparingly as a means of responding to	-

			the wrong way. (Page 797)					aggressive behaviour… it was evident that staff had communicated this philosophy to relatives. (Page 798)	
Harding (2013) [30]	-	-	-	*"I did speak with Dr [name] about the drug [antipsychotic] he'd prescribed he said it was for my dad's depression (my dad has never suffered from depression) … I went to my dad's doctor and strongly requested that my dad came off this drug … I was angry that this drug was given to my dad in the first place. I think some doctors and nursing staff have very little knowledge if any about caring for dementia people." (Family Carer) (Page 259)* Several carers attributed the prescription of antipsychotics to a lack of knowledge, training, or awareness of the negative effects on people with	*"During the sixth week [of respite] she started having nightmares, and so they wanted to give her antipsychotics, and I said 'no'. But the doctor actually prescribed them, and I think she was given one tablet and it gave her the runs, and they didn't give her anymore. But as soon as they said that, I- although I wasn't fit enough to bring her home, I brought her home." (Family Carer) (Page 262)* Informal carers, including those with power of attorney, reported not being consulted prior to the use of antipsychotic medication nor given any information about the risk/benefit profile of the drugs	*"They call it Pisa Syndrome [a side effect]… Put it down purely to drugs. So care home, well it were nursing home, that Kate was in at that time, I told GP about drugs, she said 'Well I shouldn't touch her drugs.'" (Family Carer) (Page 261)*	*"I was strongly against the use of this drug [Seroquel] after it left my dad in a zombie state." (Family Carer) (Page 259)* Clearly, carers find the sedative effects of antipsychotic medication distressing and unhelpful. Perhaps more importantly, these carers' experiences highlight that the use of antipsychotic medication as a means of controlling behaviour can be experienced as harmful even in the absence of 'severe' side effects. (Page 259)	*"Another occasion he went to a unit for assessment which was totally lacking in dementia care, he was drugged [with quetiapine] and put in a nappy when he had no continence problems, he fell and sustained a head injury as a result of this so next night he was put on the floor on a mattress. When I visited the staff supposedly caring for him were sitting watching TV while he was wandering up and down in a dazed state and when I removed him the staff became very defensive and I subsequently found that this was not an isolated incident." (Family Carer) (Page 262)* The way she (the family carer) describes his (the	Our argument is that because there is a potentially higher risk of harm to patients from off-label prescription, it should be subject to greater regulatory control, and that there should be redress available where a patient is harmed as a result of off-label prescription. (page 266)

				dementia. (Page 259)	prescribed. (Page 265)			husband's) treatment… suggests that the treatment he received may have been inappropriate, and was unlikely to have been in his best interests. (Page 262)	
Janzen (2013)	*''At times there's so little staff and there's a lot of behaviours all at once. It's just kind of putting out fires and keep things rolling. '' (Registered Nurse) (Page 529)* Although staff saw [behavioral] triggers as modifiable, the staff was unable to individually minimize triggers for each resident due to competing job responsibilities. (Page 527)	Nursing staff in this study felt that they were constantly ''putting out fires'' and stated that although they usually knew why the agitation was occurring, they did not have time to address the situation until the behaviour escalated. At such a point, medications offered a more immediate and guaranteed result. (Pages 529-530)	Each successful application of NPIs improved the staffs' confidence in their ability to use NPIs effectively. (Page 530)	Although the LTC staff possessed a high awareness of common NPIs, the use of NPIs was dependent on the staffs' perceptions of the effectiveness, past success with the NPI use, and the number of other duties competing for staff's time and attention. (Page 529)	Communication within the team and sharing successful strategies increased the likelihood that NPIs will subsequently be used by other staff. (Page 529)	-	*"... the benefits [of NPIs] are [related to] quality of life which is what you are looking for. The harms [of NPIs]? I don't see any of them. I think any time you can be individually with a person, you are helping them.'' (Unit Manager) (Page 528)* Empathy of the staff appeared to coincide with openness to using NPIs. (Page 529)	*"We [nurses] are pro medicine, we are very medicine prone. Take a pill that makes it [agitation] better.'' (Registered Nurse) (Page 528)* An experienced Registered Nurse stated that relying on medications to manage behaviours was a significant part of nursing culture in LTC. (Page 528)	-
Mavrodaris (2013)	*"Often requires one to one with a particular resident. Unfortunately when we have looked to social services for extra*	-	*''Most times behavioural issues are a cry for a need. How does a person with dementia who has got a communication deficit tell you he*	A lack of clarity regarding available and suitable pharmacological and non-pharmacological management options is suggested	Improved communication and collaboration between psychiatrists, GPs and care home staff at each level of care is fundamental and	*''We find that some GPs will continue to prescribe antipsychotic medication even when not used and discarded*	According to many of the GPs an increased risk of stroke or other cardiovascular outcomes was considered a worthwhile trade-off if prescription of the	*''Often it is pressure from nursing homes or carers for medication to calm a patient down that is trigger for prescribing." (GP) (Page 36)*	It is apparent that the current recommendation by the MHRA advocating the sole use of risperidone for six week intervals is not being practiced in

	support/funding to account for needing additional care staff it has not been successful. If this arrangement was more flexible it may reduce dramatically the need for medication.''(NH Staff member) (Page 37) Access to support services was varied among participants and highly dependent on resource. All participants reported limited access to support services and the need for more funding for alternative management strategies (Page 37)		*has got a headache?" (NH Staff member)(Page 36)* In people with dementia who have behavioural symptoms and struggle to communicate, signs of other underlying are even more difficult to elucidate. (Page 36)	by this study. (Page 37)	could improve the management of people on antipsychotic therapy. (Page 37)	*every month. Saying as the psychiatrist started it they will not stop prescribing it. But then never follow it up with a referral to have the medication altered by the said Psychiatrist.'' (NH Staff member) (Page 36)* A number of GP respondents indicated that they felt responsibility regarding the prescription and cessation of antipsychotics was that of the psychiatrist. (Page 37)	antipsychotic would improve the patient's mental wellbeing and quality of life. (Page 35)	A culture of blaming was expressed in this study. GP's reported pressure from care home staff to maintain a patient on antipsychotics, whereas care home staff reported GP's insisting on maintaining use of antipsychotic therapy. (Page 37)	primary care. This indicates that GPs may be finding it difficult to manage patients with BPSD using only one drug. (Page 37)
Ervin (2014)	*''The greatest impact on good outcomes for behaviour management is time limits. Nurses are always under pressure to hurry. We need more staff allocated to*	*''…I feel others miss out while time is devoted to the person with behaviour.'' (NH Staff Member) (Page 204)*	*''Nurses need more training in behaviour management.'' (NH Staff Member) (Page 204)* Staff education as a limitation to using behaviour oriented	Staff reported that they would treat BPSD which is unlikely to respond to antipsychotics and also reported withholding antipsychotics when BPSD indicate its use. It is reasonable	-	*''Diversional Therapy [DT] is responsible for these [cognitive-orientated] therapies as nursing staff are too busy with personal care. Behaviours*	*''Risk factors associated with antipsychotics include falls, decreased mobility and weight loss due to drowsiness.'' (NH Staff Member) (Page 203)*	Staff rarely used person-centred care terminology, indicating a lack of these practices. (Page 205)	-

	spend time with residents who have behaviour problems.''(NH Staff member) (Page 205) Time constraints were often voiced as a reflection of general poor staffing levels in Residential Aged Care Facilities and unworkable nurse/patient ratios. Time constraints may therefore also contribute to the high use of antipsychotic administration. (Page 206)		strategies was often cited. (Page 204)	to assume that poor staff knowledge of appropriate use of antipsychotics may underlie the high rate of administration, despite the reported limitations to its use. (Page 206)		*increase in severity on weekends when DT is absent." (NH Staff member) (Page 204)* Care staff viewed cognitive and stimulation management strategies as being outside their usual role, and the domain of Diversional therapy staff. (Page 206)	Adverse drug effects for residents were reported as a limitation to using antipsychotic medications as a behaviour management strategy. Respondents were concerned with issues such as drowsiness and falls resulting from antipsychotic drug administration. (Page 203)		
Smeets (2014)	*"If everyone would have one-on-one care, the problem behaviour might become something of the past." (Physician) (Page 838)* It was felt that the number of nurses or other personnel was insufficient to spend enough	*"That gentleman is so restless and they are all getting crazy and something must happen, NOW. That is how it goes." (Physician) (Page 838)* .	*"I think …that there is a very hesitant reaction to problem behaviour by the nursing staff. That in general there is little knowledge and few skills related to dementia and types of dementia. Thus, the reason it is often perceived as difficult." (Physician) (Page 838)*	Unfounded high expectations on effectiveness by nurses or family, and inadequate knowledge of dosing mechanisms by nurses may induce (additional) PD prescription… Additional reluctance may result from limited knowledge in the public field: on the mechanism of	*"At a certain moment we started having some kind of meetings…purely to discuss the residents…By jointly looking at the problems and by learning from each other…we gained more clarity, much more peace, and also had a significant decrease in prescribed medication."*	*"Look, a physician does not see the residents, I see them all day long. We, altogether, see a resident 24 hours per day, so if we accurately register their behaviour, then . . . The physician is very reliant upon us." (Nurse) (Page 838)*	*"Because you simply are afraid that the same behaviour will come back. And at that moment, you are actually glad someone is doing well. And then you think like, gosh, should you take the risk to - so to say - stop and see [does] the problems return?" (Physician) (Page 838)* Once residents are using PDs and the NPS	*"Personally, I have the feeling that the tendency is to prescribe less PDs and less quickly. As little as possible, actually; the less the better. This is, in my opinion, also something of my generation." (Physician) (Page 839)* Participants thought the public tends	Physicians expressed ambivalence about the influence of the Dutch professional guideline. According to some, it limits PD prescription; others believe that when followed routinely and interpreted as "allowance" to prescribe PDs, it stimulates prescription. (Page 839)

	time with residents for giving real attention, and providing distraction and activities. Nurses estimated that this affects the need for Psychotropic drugs (PD), especially at sundown and during night shifts. (Page 838)		Participants saw a clear relationship between knowledge and experience, primarily of nursing staff, and the need for PDs. There seems to be a greater need for PDs in cases where nurses have limited knowledge, either or not from formal education, on the nature and occurrence of NPS or less experience in managing NPS. (Page 838)	action of PDs, lack of data on PDs in the NH population, and the impression that trials are selective and test only PDs in the business interests of pharmaceutical companies. (Page 838)	*(Physician) (Page 838)* Participants felt that effective communication and cooperation between professionals may prevent occurrence or escalation of Neuropsychiatric symptoms (NPS), thereby avoiding the need for prescription of PDs. (Page 838)	Both nurses and physicians emphasized the importance of clear reporting by nurses of occurrence and severity of NPS because physicians mostly use this as a base to decide on starting PDs. (Page 838)	are… no longer perceived as too troublesome, there is a preference to continue. There can even be resistance from nurses and family to withdraw PDs, especially when considerable effort was put into stabilizing the NPS. (Pages 837-838)	toward critical scrutiny, which possibly leads to a withdrawal of PDs; they assumed that the *zeitgeist* favors limiting the prescription of PDs. (Page 839)	
Bonner (2015)	Staff and leaders of facilities with lower antipsychotic medication use consistently identified social services as having an influence on decision-making regarding antipsychotic medication use. Staff and leaders of facilities with high antipsychotic medication use tended to identify consultant psychiatry more often than staff from lower-use	-	-	The wide variety of rationales found in this study for prescribing antipsychotic medications suggests that NH teams articulate and understand the rationales for their use poorly. The dominance of poorly described behavioral and emotional explanations is a particular concern because, in many cases, safer alternatives exist for managing these	Families of residents in NHs with lower use of antipsychotic medications were more likely to indicate that they knew when the medication was started. (Page 306)	-	-	-	Off-label uses for "behaviours" in general, emotional states… and "cognitive diagnoses or symptoms" [as reported] are generally not considered to be appropriate clinical indications for antipsychotic use under current federal NH guidelines unless specific criteria are met. (Pages 306-307)

	facilities as having an influence. (Page 306)			problems. (Page 307)					
Ellis (2015)	*"[We need] improved reimbursement to allow additional staffing to provide around the clock person-centred care in our dementia unit." (Director of Nursing) (Page 513)* Our respondents highlight an important tension within NH care; the challenges of improving care within current budgets. Limited reimbursement dictates the available resources and potentially inhibits NHs' ability to adapt new practices and to acquire staff with mental health expertise. (Page 514)	-	Comprehensive skills training presented within a systematic framework is required for meaningful, sustained… improvements in care practices. Skills training must be ongoing, involve hands on supervision and be provided immediately to all new NH staff due to high volume of staff turnover. (Page 515)	*"[We need to] educate physicians that the use of antipsychotics are not the answers for residents with dementia/ behaviours... more understanding that activities are needed on a regular basis for dementia residents." (NH Risk Manager) (Page 512)* Concerns were voiced that physicians were not aware of the dangers of Antipsychotic medications for residents with dementia and did not promote non-pharmacological interventions for residents with dementia. (Page 512)	*"I would like to see hospitals be part of this process. Too often residents come to us with anti-psych meds and they seem to remain with the resident." (Director of Nursing) (Page 513)* Improvements in coordination between hospitals, assisted living facilities, physicians, and NHs were cited as ways to help NHs achieve their reduction in antipsychotic rates. (Page 513)	Surprisingly there was little to no mention of the role of certified nursing assistants… It is important, however, to emphasize the exclusion of certified nursing assistants from care teams is one of the greatest impediments to person-centred care and alienates one of the richest sources for the promotion of person-centred and individualized care. (Page 514)	NH administrators and Directors of Nursing often stated they want residents to be on the lowest dose [of antipsychotics] possible. (Page 511)	-	*"We have renewed our focus and utilize an interdisciplinary team approach to reduce [antipsychotics]." (Nursing Home Administrator) (Page 511)* This study explores how NHs responded to the 2012 [Centres of Medicare and Medicaid] CMS initiative to reduce inappropriate antipsychotic use among residents… Results confirm the majority of NHs are actively working to reduce unnecessary antipsychotic medications. (Page 513)
Lawrence (2016)	*"There has been so much focus on it recently, dealing with challenging behaviour,*	*"You feel like you're not doing your job properly. You actually feel that you're letting the residents down.*	*"Some of them can be quite aggressive if they won't take that medication [antipsychotic], and*	*"It will really help to raise awareness among them [the prescribing GP] because they would*	*"We all work as a cog in a wheel and if one of those cogs breaks then the wheel doesn't turn*	*"Some of them have the attitude, 'It's [performing NPI] not my job, I am just here to*	*"Most of them you see them drowsy at times, at times it is a sedative, I wouldn't like antipsychotics or*	Three focus groups confided that medication was sometimes necessary for the	-

	creating different activities, etc… but what people need to realise is that to do that costs a lot more money. To give one to one intervention is very expensive. Whereas it's dead easy isn't it if you give them a few tablets?" (NH Staff member) (Page 286) Insufficient resources were presented as an enduring barrier to implementing person-centred care, reducing anti-psychotic medication and undertaking activities within the workplace. (Page 291)	*Yeah that you're letting them down. You say, 'I'll be with you in a minute, I'll be back'…and you're not, you're running off for something else." (NH Staff member) (Page 286)* Low staffing numbers and a perceived rise in the proportion of residents with dementia contributed to the view that 'physically and mentally it is draining'. Participants explained that being 'fully staffed, but understaffed' limited their involvement in activities, the feasibility of spending one-to-one time with residents and their ability to implement person centred care. (Page 288)	*it's how to deal with the aggression from them because we can all do 'Yesterday, Today and Tomorrow', which is a lovely course, it is brilliant, but we never actually had training where I worked of how to deal with the aggression side of it." (NH Staff member) (Page 287)* We found cautious enthusiasm for training interventions that promise to help staff implement psychosocial interventions within their everyday work. (Page 292)	*never change the medication if it weren't for this." (NH Staff Member) (Page 287)*	*does it? So what we do is we all work together it's like they work upstairs with the carers and if something is wrong they report here and then it gets reported to the doctor." (NH Staff member) (Page 287)* The cohesiveness of staff within the care home was considered key to the provision of high-quality care. Three groups argued that the shared ethos of the team helped to mitigate the challenges posed by time pressures and low staffing numbers. (Page 288)	*clean him, feed him, that's it, I don't need to do anything else, it's not my job'." (NH Staff Member) (Page 287)* A recurring issue was the potential disjuncture between carers, who in some instances seemed to provide the majority of daily care, and nurses, who were responsible for writing care plans and daily reports… (Page 288)	*wish…so they need to review and do something about it." (NH Staff member) (Page 287)* Participants in roughly half the care homes hoped that the training programme would help to reduce the use of antipsychotics within the home. (Page 289)	care home itself, as it was not always possible to give residents the "positive attention" that was needed to avert aggressive behaviour. Some participants were uncertain how they would have time to attend to residents if antipsychotics were reduced. (Page 289)	
Sawan (2016 A)	GP participants who opted not to attend routine MAC [Medication Advisory Committee] meetings explained that they were limited by time and other work	-	-	*"We ensure that at our [MAC] meetings we have the [accredited] pharmacists there and involve them in discussions on psychotropics." (Nursing Home Manager) (Page 1730)*	*"There are some families that say, 'you think it [psychotropic medication] might be too much? Every time I come and visit, he's just sleeping or is just not into it'. We say to them 'if you are*	*"We go to MAC meetings because that's an opportunity to meet a couple of GPs… I'm meeting exactly the same GPs every time." (Geriatrician) (Page 1730)*	-	*"Everybody else raised the issue (at the MAC) of no 'PRN' [when required] psychotropic medications and to reduce the load of medications including*	Although it is a requirement for Australian nursing homes that every resident receives a Residential Medication Management Review [RMMR] as soon as possible after admission or on a

	commitments such as managing their own surgeries... As a result, discussions on the appropriate use of psychotropic medicines were not conveyed to all GPs. (Page 1730)			[In this Australian setting] In all, but one nursing home, accredited pharmacists'… participation in MAC meetings was considered important for guidance on the use of psychotropic medicines, given their extensive knowledge of pharmacotherapy. (Page 1729)	*really concerned, then we will get the doctor to review it again.'" (Healthcare Assistant) (Page 1731)* Some families highlighted concerns to on-site staff…The concerns of families would be noted by on-site staff to request the GP to review psychotropic medicines. (Page 1731)	GPs are responsible for the vast majority of prescribing in nursing homes; however, most nursing homes indicated that it was difficult to organize GP attendance at MAC meetings. (Page 1730)		*psychotropics." (GP) (Page 1729)* Our study identified MAC meetings as an important artefact of organizational culture related to the use of psychotropic medicines in nursing homes. (Page 1732)	clinical needs basis to current residents, we found variability in the way nursing homes utilized the specific recommendations from the RMMRs. (Page 1730)
Sawan (2016 B)	*"The desire to make money means that they [nursing homes] have to make choices about staffing levels and staffing quality that is good for the money making side but not necessarily good for the patient side. Then of course they might want shortcuts to enable them to cope with the less qualified staff or the less numbers of staff. That's*	*"Staff often reported feeling frustrated as the care that should be provided is not being given due to insufficient staff hours, insufficient staff, lack of specialized training; because they only had minimal basic training, and because they found it difficult to deal with increased care needs." (Registered Nurse) (Page 5)* These perceptions [of feeling overwhelmed and unqualified to handle residents with BPSD] were more	*"In the nursing home, it is very hard to use the other means to help with sleeping problems. After giving a few weeks' trial off [the psychotropic medicine], the staff keep on telling me that they're not able to cope with the patient, so what do you do? The employees are not as well trained to handle these kinds of patients." (GP) (Page 5)* A number of visiting staff perceived that	*"We are not supposed to know what it [psychotropic medicine] is or what it does. We're just people who give the medication." (Nursing Assistant) (Page 6)* Some nursing assistants felt that their involvement was not supported by their manager as they were expected to not know the indications of psychotropic medicines. In other cases, they felt	*"Nursing Home X is open to having us communicate with doctors if we can, and trying to reduce medication load for all their patients. That's one of the manager's main focuses there, trying to reduce psychotropics and polypharmacy, so they want us to be involved in meetings and try to reduce medication burden for their residents." (Pharmacist) (Page 6)*	*"If I see residents' behaviour is different, they're more restless, more agitated, anything that I notice that is not normal, I'll tell them." (Nursing Assistant) (Page 6)* Some nursing assistants mentioned that they were supported by their managers to report resident observations and response to psychotropic	*"They're the necessary evil [psychotropic medication]. Sometimes we do have to use it for behaviour. Sometimes it's not appropriate but you have the nursing staff requesting it to calm down the patients. Sometimes you use it unnecessarily a bit longer than we should." (GP) (Page 5)* The majority of GP participants viewed psychotropic medicines as a 'necessary evil' to deal with the high	*"[Manager of Nursing Home Y] has a unique appreciation for the diversity of personality and character in the world and she actually celebrates this. She is far from normal and average in this industry. Staff are never asking me to sedate – they're never asking me for sleepers. It's a whole different world so actually I'm really at one with them. They will tell me that they're worried that Mrs.*	-

	where controlling and managing the patient might come in." (GP) (Page 6) Some visiting staff perceived that it was the prioritization to make profit by the nursing home providers which created shortages in staff levels and staff skill mix. This created the work distress and workload for on-site staff in handling residents with behavioral and sleep disturbances and using psychotropic medicines as a coping mechanism. (Page 5)	pronounced in low care nursing homes with 'ageing in place' where residents would be permitted to remain in care even if their needs increased over time from low to high. (Page 5)	in some nursing homes the non-pharmacological management of BPSD and insomnia was limited due to minimal staffing and on-site staff not being adequately trained to address behavioral disturbances. They felt psychotropic medicines were often requested by on-site staff as a solution to their distress from dealing with behavioral disturbances. (Page 5)	uncertain about their ability to participate because of their level of medical knowledge. They therefore did not provide input in care decisions involving psychotropic medicines. (Page 6)	The findings of this study suggest nursing home managers who clearly communicate priorities for the non-pharmacological management of behavioral disturbances and encourage staff participation in monitoring and review of psychotropic medicines influence the use psychotropic medicines. (Page 8)	medicines. They felt that they were listened to by their managers (and RNs) and felt empowered to report any changes in the residents' condition as they were encouraged to follow their intuition. Participation in the monitoring of psychotropic medicines contributed to the review and cessation of psychotropic medicines. (Page 6)	workload of on-site staff due to lower staffing levels, primarily during the night. They reported to receive requests for the initiation of psychotropic medicines to address night time behavioral disturbances. Additionally, psychotropic medicines were seen to be required for the sake of peace and calm for on-site staff and other residents. (Page 5)	*Blogs is too sluggish." (GP) (Page 6)* The study found that managers' attitudes toward psychotropic medicines were critical as it also established the standards for accepted practices for the management of behavioral and sleep disturbances by on-site staff, either hindering or facilitating appropriate use of psychotropic medicines. Managers' knowledge and understanding of the potential harm associated with psychotropic medicines may be linked to these attitudes. (Page 8)	
Shaw (2016)	*"If they just would put an extra member of staff on each shift, it would make an awful lot of difference." (Care Assistant) (Page 126)*	-	*"In place of zopiclone or temazepam, it would be repositioning them overnight, checking incontinence is cared for, that the room is*	*"There are some GPs who is not well versed with the dementia…they prescribe anything and everything under the sun." (Nursing Home*	*"The staff, the patients, the families and everybody interact together with the patient as the main focus." (Nursing Home Manager) (Page 127)*	*"It'd be my saying…that I don't think this is right for this person…but who are we to argue with the higher [prescribers]?" (Nursing Home*	*"Their behaviour is just, like, really annoying." (Nurse) (Page 126)* The attitudes of nursing home staff towards residents with dementia may	*"[Nursing homes] always need to have some sort of routine…so if one person does one thing that way, then everybody else will participate and do exactly the same*	-

	Staffing levels were generally seen as problematic, potentially leading to use of a psychoactive medication. This reflects previous findings, which suggested that homes used psychoactive medications to substitute for inadequate staffing levels. (Page 128)		*comfortable, things like that." (Nurse) (Page 126)*	*Manager) (Page 127)*	Effective working relationships with physicians and other healthcare team members are critical to success (Page 128)	*Manager) (Page 127)* Participants from traditional [culture] nursing homes appeared to be dissatisfied with prescribing outcomes yet felt unable to approach the prescriber to discuss it, possibly because they had a poorer relationship with the prescriber. Thus, the quality of the relationship between the staff and the prescriber appeared to influence whether nursing home staff were involved in decision making. (Page 129)	influence how they are treated… This seemed to be borne out by staff in traditional homes; one participant saw older people with dementia as ''annoying'' and went on to say they would be given a psychoactive medication, which was beneficial for them. (Page 128)	*thing…and, to be honest with you, I think it's good for them, the residents, to have routine as well." (Care Assistant) (Page 125)* Traditional [culture] homes' staff expressed the need for certain routines to be carried out... Participants placed importance on having set meal times and bed times, and showed a regimented approach to daily living, with little flexibility. (Page 128)	
Van Wyk (2016)	Participants in this study indicated the need for more staff so that they could spend more time with residents with dementia, especially those with distressed behaviour. They reported that it	*"They will attack you, be aggressive, grab you, pinch you and spit at you. It is not always easy." (Care assistant) (Page 6)*	*"I did a workshop, it wasn't too involved, only one day, but it really helped me. I am calmer and know better what to do. Before I had the training I would just pick up and go, but now I know you have to first tell the person what you are*	The majority of participants had basic school education and little or no dementia training. (Page 7)	-	Some care home managers were said to limit access to residents' personal files to the Sister in charge, this was indicative of other data in the interviews of a hierarchical	*"Sometimes they are so overmedicated and are like 'zombies'. It is not nice if they are like that, because you cannot work with them if they are in that state." (Care assistant) (Page 7)* Participants thought that doctors often	The findings suggest that staff in care homes varied in their perceptions of working with people with dementia, but there were not many within-home differences. These aspects could be indicative of the	-

	takes longer to care for people with dementia as they need more time to understand and co-operate with care than other residents. (Page 9)		*going to do, not just go ahead and do." (Care Assistant). (Page 7)* There seemed to be consensus among care staff that dementia-specific training would greatly benefit their practice and enhance their ability to provide care with confidence. (Page 10)			'divide' between care staff and management. (Page 9)	prescribed too high doses of tranquilisers resulting in unresponsive residents who were difficult to work with. The use of medication and restraint was reportedly to be a last resort if interpersonal approaches were ineffective. (Page 7)	leadership and culture in these homes, contributing to staff satisfaction and morale. (Page 8)	
3rd Order Interpretation	• Chronic under-staffing is a fundamental issue in NHs, leading to insufficient time and ability by NH staff to perform person-centred care • The involvement of specialist services can influence antipsychotic prescribing, but sometimes there can be difficulty accessing these services • To circumvent the problems of inadequate resources and/or poor access to specialist services, antipsychotics are 'employed' as cheap, fast and effective staff members. • As behaviours escalate, a 'tipping-point' is reached, after which an urgency to resolve the situation arises. This is particularly true when NH staff feel "overwhelmed" by these behaviours. In these situations antipsychotics are perceived by NH staff to offer a "more guaranteed result" • The perceived acuteness of situations forces NH staff to focus		• Both prescribers and NH staff are often perceived to be poorly equipped to deal with BPSD in terms of deficiencies in dementia-specific skills and/or a lack of knowledge on the risk/benefits of antipsychotics, and the range and nature of NPI. These deficiencies enable inappropriate antipsychotic prescribing. • More training and education to help prescribers and NH staff to improve skills and knowledge with regards to BPSD management is desired • Even in individuals with sufficient skills and knowledge regarding BPSD management, a tension can exist between 'doing the right thing' and doing what's practical, especially if the resources or suitable alternatives are not perceived to be there to support adequate implementation • Knowing the resident and understanding their behaviours contributes towards successful BPSD management		• Effective communication and collaboration (involving sharing information and listening to others) between all members of the healthcare team are key enablers to reducing inappropriate prescribing of antipsychotics. The involvement of family members can also be important in this process • A lack of empowerment at all levels of the healthcare team and among family members is a barrier to informed decision-making regarding antipsychotic prescribing • Fragmentation between different levels of care creates confusion surrounding roles and responsibilities, which can lead to inappropriate maintenance of antipsychotics		• Although there is a preference to use NPI in the first instance due to the unpleasant side effects of antipsychotics, it is acknowledged that antipsychotics are a "necessary evil" and are often unavoidable • Negative attitudes by individuals towards people with dementia can result in inappropriate antipsychotic prescribing. Conversely, empathy towards people with dementia can be protective • Fear of the recurrence of behaviours motivates maintenance of antipsychotic prescribing • Organisational and societal attitudes towards people with dementia and the management of BPSD, exerts pressure on prescribers to make prescribing decisions • The attitude of the NH manager towards people with dementia and the management of BPSD dictates the treatment culture of that NH, and this has a strong influence on antipsychotic prescribing		• Regulations are perceived to be the driving force for antipsychotic reductions in NH residents with dementia, but adherence to them can be challenging • Guidelines exert little influence on antipsychotic prescribing, but may act indirectly to increase knowledge regarding the risk/benefits of antipsychotics.

	their attention on the "aggressive" residents, while the "passive" ones are left behind. Antipsychotics can sometimes be viewed as a way of equalising attention given to both "passive" and "aggressive" residents			• Tensions can arise due to incompatible beliefs towards antipsychotics between prescribers and NHs; in these cases a battle of wills develops where there is often pressure on prescribers to "do something" in order to restore control – doing nothing is not tolerated. However, sometimes there is pressure on prescribers to discontinue antipsychotics, to which there can be resistance from prescribers	

BPSD, Behavioural and Psychological Symptoms of Dementia; NPI, Non-pharmacological interventions; LTC, Long-term care; NH, Nursing Home; SCU, Specialist Care Unit; GP, General Practitioner; CAN, Certified Nursing Assistant; OBRA, Omnibus Budget Reconciliation Act; MHRA, Medicines and Healthcare products Regulatory Agency; DT, Diversional Therapy; PD, Psychotropic Drugs; NPS, Neuropsychiatric Symptoms; MAC, Medication Advisory Committee

Appendix 5. COREQ Checklist for Chapter 5

Domain 1: Research team and reflexivity			
Personal Characteristics			
1.	Interviewer/ facilitator	Which author/s conducted the interview or focus group?	KW conducted the interviews
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD*	At the time of undertaking the interviews KW's credentials were *BPharm, MPharm, MPSI*
3.	Occupation	What was their occupation at the time of the study?	KW is an Irish registered pharmacist, who was undertaking a PhD in Population Health and Health Services Research, when this study was conducted.
4.	Gender	Was the researcher male or female?	Male
5.	Experience and training	What experience or training did the researcher have?	KW completed training in utilisation of NVivo software and received qualitative research methods training at Oxford University, UK. KW has also conducted and published a systematic review and synthesis of qualitative evidence previously.
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement?	There were no established relationships between any of the 27 participants and the researcher or research team prior to study commencement.
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.*g. personal goals, reasons for doing the research*	KW had disclosed to all participants that he was a pharmacist undertaking this study as part of his PhD, prior to conducting the interviews.
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic*	KW is a registered pharmacist with community pharmacy and qualitative research experience, and was conducting this study as part of his PhD exploring antipsychotic prescribing in nursing home residents with dementia. This information was disclosed to participants ahead of the interview. In order to minimise the potential for KW's information bias, entering the analysis, a mix of professionals (clinical and non-clinical) were involved in the analysis, with varying levels of knowledge on this specific topic. Our research team consisted of a broad range of disciplines: pharmacists (KW, AF, SB); a general practitioner (CS); a health psychologist (JMcS); a methodologist (JB); and a geriatrician (ST). Triangulation of analysts contributed toward the credibility of the results, and minimised bias from any one particular researcher.
Domain 2: study design			
Theoretical framework			

9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis*	Framework Analysis as described by Ritchie and Lewis, utilising the *Theoretical Domains Framework* (TDF) as the *a priori* defined framework.
Participant selection			
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball*	Participants were purposively sampled to ensure a heterogeneous group with maximum variation according to two main pre-determined criteria *(Professional/social role and nursing home type*). We also used snowball sampling to fulfil our sampling framework requirements. Six different nursing home sites were selected based on our sampling framework, through publicly available directories of registered nursing homes on the Health Information and Quality Authority (HIQA) and Nursing Home Ireland websites
11.	Method of approach	How were participants approached? e.*g. face-to-face, telephone, mail, email*	The Directors of each nursing home (Directors of Nursing or Medical Directors) were contacted by KW by email initially and informed about the study, with a follow up phone-call if no response. Once the Directors agreed access, they were interviewed themselves by KW and they then recommended other potential participants connected to their nursing home, whom KW would approach face-to-face or via email/telephone with information about the study. All relevant visiting staff (i.e. GPs, consultant psychiatrists of old age, consultant geriatricians and pharmacists) serving each of the sites were invited to participate in the study. The Directors approached family members initially about the study before recommending to KW that they were suitable to be contacted.
12.	Sample size	How many participants were in the study?	27
13.	Non-participation	How many people refused to participate or dropped out? Reasons?	Of 6 nursing homes contacted by KW via their respective Director, 4 participated and 2 did not respond. Of the 4 pharmacists serving the 4 different nursing home sites, 2 participated. 1 said they was too busy and 1 did not respond. Of the 9 GPs serving the 4 different nursing home sites, 5 participated. 2 initially agreed but never followed up with a definite date for interview and 2 did not respond. Of 10 nurses across the 4 different sites who were contacted by KW, 8 participated. 1 said they were too busy and 1 did not respond. Of 5 family members who were contacted by KW, 3 participated. 1 initially agreed but never followed up with a definite date for interview. 1 initially agreed but then cancelled because the rest of the family didn't want to be involved. An unknown number of family members were informally approached about the study by the

			Directors of each nursing home site, but did not agree to participate. Of 3 Consultant Geriatricians contacted by KW, 2 participated. 1 initially agreed but never followed up with a definite date for interview. Of 2 Consultant Psychiatrists of Old Age contacted by KW, both participated. Of 5 Healthcare assistants contacted by KW, all 5 participated. **Total non-participators:** n=2 nursing homes, n=11 individuals directly contacted by KW
Setting			
14.	Setting of data collection	Where was the data collected? e.*g. home, clinic, workplace*	All interviews took place either in the participant's place of work, home or an office in the researcher's university, depending on participant's preference.
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? *e.g. demographic data, date*	Refer to table of demographics in Chapter 5
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Three types of topic guides were in circulation at any one time. They were broadly similar for content, but differed primarily for language: • 1 for healthcare professionals (physicians, nurses, and pharmacists), • 1 for healthcare assistants • 1 for family members. The topic guides were pilot tested by 5 participants (1 nurse, 1 healthcare assistant, 1 pharmacist, 1 GP and 1 family member) to ensure appropriate content and language for the different groups. All topic guides were revised slightly after every pilot interview. Only the latter interview conducted with a family member was subsequently included in the analysis, as this topic guide was agreed to be close enough to the final version. Throughout the remainder of the study, the topic guides underwent iterative revision to ensure that emerging themes were captured in subsequent interviews.
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many?	No

19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?	All interviews were audio recorded.
20.	Field notes	Were field notes made during and/or after the interview or focus group?	Field notes were written immediately after the interviews, and were referred to during analysis, and refinement of topic guides.
21.	Duration	What was the duration of the interviews or focus group?	The median interview length was 23 minutes and the range was 12-56 minutes.
22.	Data saturation	Was data saturation discussed?	The Francis *et al* method was used to determine when data saturation had been reached. We sampled until no new ideas emerged from the interviews and then conducted a further three interviews without any new ideas emerging to ensure that data saturation had been reached.
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No.
Domain 3: analysis and findings			
Data analysis			
24.	Number of data coders	How many data coders coded the data?	Four (KW, CS, AF, JMcS)
25.	Description of the coding tree	Did authors provide a description of the coding tree?	The Theoretical Domains Framework (TDF) was used as a basis for the coding tree
26.	Derivation of themes	Were themes identified in advance or derived from the data?	We utilised both deductive and inductive approaches to analysis throughout the five framework stages (familiarisation, identifying a thematic framework, indexing, charting, and mapping and interpretation). First KW became familiar with the data by reading and re-reading transcripts and field notes and open coded across the entire dataset. The 14 TDF domains were then deductively applied systematically to the data during indexing while emerging concepts were coded and categorized inductively. These indexing steps were conducted independently by at least two authors for seven transcripts (KW and AF/JMcS), who met to discuss differences in application of the TDF or interpretation of emerging concepts, and came to consensus. The indexing of the remaining transcripts was conducted by KW using agreed understandings of the TDF domains. Charting of the data, with distilled summaries in matrix format was used to identify the predominant domains influencing the target behaviours (appropriate requesting and prescribing). This activity was performed independently by two authors (KW and CS), who then discussed any disagreement until consensus was reached. From these predominant domains, the determinants (i.e. barriers and facilitators) of the target behaviours were identified by KW, with input from the whole team. For the final mapping and interpretation step, we iteratively developed links between barriers and facilitators, predominant

			domains, initial categories and theory to provide overall explanations for the findings. This was conducted by KW, with input from the whole research team.
27.	Software	What software, if applicable, was used to manage the data?	NVivo 11
28.	Participant checking	Did participants provide feedback on the findings?	No
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.*g. participant number*	Yes
30.	Data and findings consistent	Was there consistency between the data presented and the findings?	Quotes are presented in a manner consistent with findings
31.	Clarity of major themes	Were major themes clearly presented in the findings?	Major (explanatory) themes are presented in the results section.
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	The predominant TDF domains that feed into the major (explanatory) themes are explored in detail in the results section

COREQ, COnsolidated criteria for REporting Qualitative research.

Appendix 6. Final Version of Topic Guides for Chapter 5

Healthcare professionals

1. In your own words, tell me what your views are regarding the use of antipsychotics in nursing home residents with dementia. *(Prompts: Is it appropriately prescribed in all cases? Is it necessary?) (What impact, if any, do resources and financial issues have an AP prescribing, in your experience?)*
2. In the context of NH residents with dementia, what you would you define as an "appropriate" usage of these agents? *(Prompts: indication, frequency of review, duration, who needs to be consulted?)*
3.* [If not mentioned] Can you talk me through your general approach to: prescribing (physician)/ requesting (nurses)/ dispensing (pharmacist) a prescription for, AP medications to a typical resident with dementia, who may be exhibiting behaviours that challenge? *(Rephrase: Talk me through one situation where this occurred. Prompts: How would you start this process or journey for a NH resident with dementia? What is the first thing you would always do? Use of NPI? What would you do next? Would you always do this? Anything else? What about reviewing? What about PRN usage)
4.* Can you tell me about a case where you were able to successfully reduce someone's dosage of these agents or manage someone without medications. What do you believe were the main facilitators? (What do you believe enables "appropriate*" usage?) (Rephrase: What facilitates the use of alternative non-pharmacological approaches in residents who may not necessarily need AP/P medications?)
5. Now can you tell me about a case where you were perhaps less successful. What do you believe were the main barriers in this case? How is it different? (What do you believe to be the main barriers to "appropriate" usage?) *(Rephrase: What prevents the use of alternative non-pharmacological approaches in residents who may not necessarily need meds?)*
6.* What are your views on non-pharmacological approaches? *(Prompts: Are they effective? Whose role is it? Are they being used first-line?)
7.* Do you believe that everyone involved in the care of residents with dementia knows enough about these medications? *(Prompts: Why do you think this? Is there any group of people in particular that you feel could benefit from more training and education? What specifically do you think they need to know more about?)
8.* What about having the skills to effectively manage someone who is exhibiting behaviours that challenge? *(Prompts: Why do you think this? Is there any group of people in particular that you feel could benefit from more training and education? What specifically do you think they need to know more about?)
***9.* What would you consider your responsibilities to be as a _ in ensuring that the residents receive these medicines appropriately?**
10.* [If not answered] What strategies or resources are currently available to support you in ensuring their usage is appropriate? *(Rephrase: What resources would you use/consult with first to ensure appropriateness e.g. guidelines, pharmacists, GP.
11.* As you may be aware, we are planning to undertake an intervention study in your NH to help support nurses, HCAs and doctors in ensuring prescribing of antipsychotics is to a high quality. What would you like to see in this intervention programme?*(Prompts: What would be helpful to you as a X? What would not be helpful to you?)
12.* Who would influence your decision about whether or not to prescribe an AP to a resident with dementia? What about guidelines? (Physician only) *(Prompts: Why/ Why not? Individuals/groups of HCPs/ finance/Nursing Home itself/ public opinion/guidelines. Anyone else) (Rephrase: How, if at all, does the team communicate about APM usage?)
OR

12. How do you think that your views and opinions, and that of others, influence the prescriber, in relation to AP prescribing? What about guidelines? (Nurses and Pharmacists) *(Prompts: Individuals/groups of HCPs/finance/Nursing Home itself/ public opinion/guidelines. Anyone else?)*

13. Some people say that if a healthcare professional has a greater understanding of dementia then they might be less inclined to use antipsychotics. What do you think about that?

(Rephrase: Some studies in the literature found that HCPs with a positive attitude toward PwD were less likely to use APM. Would you agree with this statement?)

***14.* Do different nursing homes have different cultures? If so, what impact does this have on AP prescribing? [If working in multiple sites]**

15. [If not mentioned already] (You may or may not be aware but HIQA have recently started conducting Dementia-themed inspections of Nursing Homes, and have released updated standards with an increased emphasis on chemical restraints.) What is your opinion on the influence of HIQA on AP prescribing in the NH setting? *Prompts: HIQA have released new updated Standards with an increased emphasis on restraint use in NH residents with dementia, are you familiar with them? Any thoughts? Negative or Positive Light?)*

16. That brings us to the end of the interview. Is there anything else I haven't asked you today that you would like to mention?

Healthcare assistants

1. In your own words, tell me what your views are regarding the use of antipsychotic medications in dementia residents who are exhibiting challenging behaviours. *(Prompts: Antipsychotics such as Zyprexa and Seroquel. Other relaxers such as Xanax or Ativan. Is it appropriately prescribed in all cases? Is it necessary? What are the benefits and harms?)*

2. In these residents, what would you define as an "appropriate" use of these kind of medications? *(Prompts: indication, frequency of review, duration, who needs to be consulted?)*

3.* [If not mentioned] Can you talk me through your general approach to requesting a prescription for these agents to a dementia resident, who may be exhibiting challenging behaviours? *(Prompts if necessary: Is that something you would normally do as a HCA? How would you start this process or journey for a NH resident with dementia? What is the first thing you would always do? Use of NPI? What would you do next? Would you always do this? Anything else? What about reviewing?)

4.* Can you tell me about a case where the team were able to successfully reduce someone's dosage of these agents and you were able to manage them without medications? What do you believe were the main facilitators? (What do you believe enables "appropriate*" usage?) (Rephrase: What facilitates the use of alternative non-pharmacological approaches in residents who may not necessarily need AP/P medications?)

5. Now can you tell me about a case where you were perhaps unable to manage the patient without some form of medication? What do you believe were the main barriers in this case? How is it different? (What do you believe to be the main barriers to "appropriate" use?) *(Rephrase: What prevents the use of alternative non-pharmacological approaches in residents who may not necessarily need meds?)*

6. What are your views on alternative approaches to managing behaviours, such as distraction, massage therapy, reminiscence therapy and music therapy? *(Prompts if required: Do they work? Whose role is it? Are they being used before medications?)*

7.* Do you believe that everyone involved in the care of residents with dementia know enough about these meds? *(Prompts: Why do you think this is? Is there any group of people in particular that you feel could benefit from more training and education? Consultants, GPs, Nurses, Pharmacists, HCAs and family members. What specifically do you think they need to know more about?)

8.* What about having the skills to effectively manage these challenging behaviours? *(Prompts: Why do you think this is? Is there any group of people in particular that you feel could benefit from more training and education? What do you think they need to know more about?)

***9.* What would you consider your responsibilities to be as a HCA in ensuring that all residents receive these meds appropriately?**

10. **[If not answered] What strategies or resources are currently available to support this nursing home in ensuring the usage of these meds are appropriate?** ***(Rephrase: What resources would they use/consult with first to ensure appropriateness e.g. guidelines, pharmacists, GP.***
11. **As you may be aware, we are planning to undertake an intervention study in your NH to help support nurses, HCAs and doctors in ensuring prescribing of antipsychotics is to a high quality. What would you like to see in this intervention programme?** ***(Prompts: What would be helpful to you as a X? What would not be helpful to you?)***
12. **How do you think that your views and opinions, and that of others, influence the prescriber, in relation to AP prescribing?** ***(Prompts: Individuals/groups of HCPs/ finance/public opinion/guidelines. Anyone else?)***
13. Some people say that if a healthcare professional has a greater understanding of dementia then they might be less inclined to use antipsychotics. What do you think about that?
(Rephrase: Some studies in the literature found that HCPs with a positive attitude toward PwD were less likely to use APM. Would you agree with this statement?)
14. **[If not mentioned already] (You may or may not be aware but HIQA have recently started conducting Dementia-themed inspections of Nursing Homes, and have released updated standards with an increased emphasis on chemical restraints.) What is your opinion on the influence of HIQA on AP prescribing in the NH setting Strategy?** ***(Prompts: HIQA have released new updated Standards with an increased emphasis on restraint use in NH residents with dementia, are you familiar with them? Any thoughts? Positive or negative light?)***
15. That brings us to the end of the interview. Is there anything else I haven't asked you today that you would like to mention?

Family Members

1. In your own words, can you describe what your views are towards the use of medications in the care of your loved one? ***(Prompts if necessary: have they been beneficial? Have you noticed any improvements? Have they caused any side effects?)***
The focus of my PhD research is on the usage of a group of medications called Antipsychotics in NH residents with dementia. Common examples of Antipsychotics include Zyprexa, Seroquel and Serenace. These drugs are sometimes prescribed to people with dementia if they are severely distressed or displaying some behaviours that others may find challenging such as aggressive or agitated behaviour.
2. **If you have any experience in the use of these medications in your loved one, I'd be very interested to hear your story. (If not, then this is absolutely fine we can still talk about medication use in general)** ***(Prompts if necessary: Why was he/she prescribed these drugs? Can you remember what it was he/she was prescribed? Did it help the situation? Were there any side effects? Is he/she still on it? Who stopped it and why?)***
3. **Whenever your loved one is a bit agitated or distressed, is there anything that helps to put them at ease?** ***(Prompts if necessary: Reminiscing about the past? Activities? What about Medications?)***
4. Have you ever requested a prescription for such a medication or have you ever requested it to be stopped or reviewed? If yes, could you describe for me in general what happened? ***(Prompts if necessary: Why did you do this? Is that something you would normally do as a family member? Would you always do this? Anything else?)***
5. **From your perspective, what would constitute an "appropriate" use of such a medication?** ***(Prompts if necessary: Who needs to be consulted in the process? How long should they be on it, in general?)***
6. **What are your views on alternative approaches to managing behaviours, such as massage therapy, reminiscence therapy and music therapy?** ***(Prompts if required: Do they work? Whose role is it? Are they being used before medications?)***
7. **Do you believe that everyone involved in the care of residents with dementia know enough about these drugs?** ***(Prompts if necessary: Do family members know enough? Should they know more? Is there any group of people in particular that you feel could benefit from more training and education? What specifically do you think they need to know more about?)***
8. What about having the skills to effectively manage someone who is exhibiting behaviours that challenge? ***(Prompts if necessary: Without using medicines. Why do you think this? Is there any group of people in particular that you feel could benefit from more training and education? What do you think they need to know more about?)***

9. **What would you consider your responsibilities to be as family member in ensuring that he/she receives an appropriate prescription of these medications?**
10. How do you think that your views and opinions, influence the GP, in relation to prescribing of these agents? What about the views of others? (Prompts if required: Individuals/groups of HCPs/financial/ public opinion/guidelines/ dementia strategy. Anyone else?, *How are your views and opinions communicated to the GP?*
11. Some people say that if a healthcare professional has a greater understanding of dementia then they might be less inclined to use antipsychotics. What do you think about that?
(Rephrase: Some studies have found that HCPs with a positive attitude toward PwD were less likely to use APM. Would you agree with this statement?)
12. That brings us to the end of the interview. Is there anything else I haven't asked you today that you would like to mention?

Appendix 7. TIDieR Checklist for Chapters 6/7

Item number	Item	Description
BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	The *'Rationalising Antipsychotic Prescribing in Dementia'* (RAPID) complex intervention.
WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	The RAPID complex intervention was developed using the Behaviour Change Wheel approach and was informed through theory (Theoretical Domains Framework) and evidence (qualitative and quantitative). The overall aim of the intervention is to improve the appropriateness of antipsychotic requesting and prescribing for nursing home residents with dementia.
WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	The RAPID complex intervention includes 3 main components: 1. Education and training sessions with nursing home staff 2. Academic detailing with GPs 3. Introduction of an assessment tool (the RAPID assessment tool) to the nursing home environment Materials provided for each component: 1. The education and training sessions: Written educational material discussing 4 topics will be provided to participants (understanding and responding to the person with dementia, everyday ethics, antipsychotic drug use in dementia, and understanding emotion). The RAPID assessment tool (paper-based) along with sample case studies (paper-based) will also be provided to participants. A facilitator's guide will be provided to facilitators. 2. Academic detailing: A paper-based guidance document discussing appropriate antipsychotic prescribing will be provided to GPs. The RAPID assessment tool will also be provided 3. Introduction of an assessment tool: The RAPID assessment tool will be provided to all participating wards. Further details on the materials used can be found in the attached CD-ROM (Appendix 8).

4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	The procedures involved in the RAPID complex intervention are as follows (the 16 relevant behaviour change techniques [BCTs] are italicised in brackets): • The five intervention functions directed at nursing home staff will include: **Education, Training, Persuasion, Environmental Restructuring and Modelling**. • During education and training session, nursing home staff will be provided with written and oral information regarding the risks and benefits of antipsychotics *(5.1 Information about health consequences)* from experienced pharmacists and nurses *(9.1 Credible source).* After presenting the evidence, staff will be asked to consider antipsychotics as the last resort when dealing with the majority of behavioural symptoms, rather than the first-line treatment *(13.2 Framing/re-framing)* and will be encouraged to use non-drug alternatives instead of requesting antipsychotics in these instances *(8.2 Behaviour substitution).* Through group discussions, staff members will share with each other, occasions where non-drug strategies worked and antipsychotics were not needed *(15.3 Focus on past success).* • At the same education and training session, nursing home staff will be introduced to the newly developed RAPID assessment tool which has the aim of aiding staff with the assessment of behavioural symptoms and ultimately reduce inappropriate requests for antipsychotics. Staff will be directed how to complete the RAPID tool via demonstration *(6.1 demonstration of behaviour)* and also through written instructions accompanying the tool *(4.1 Instruction on how to perform a behaviour).* The RAPID tool will focus staff's attention on identifying and exploring patterns of events and triggers that occur in residents (e.g. repetitive actions, sun-downing, pain) *(4.2 Information about antecedents)* that may ultimately lead to an inappropriate request for an antipsychotic, and to develop non-drug strategies to use in these situations to address these factors *(1.2 Problem solving).* Staff will be encouraged to outline a detailed plan of how and when non-drug and/or drug interventions will be utilised in such situations *(1.4 Action Planning)*. Staff will practice using the RAPID tool based on case studies provided in the education and training session *(8.1 Behavioural practice/rehearsal).* Staff who have attended the education and training session will be encouraged to use this tool and apply this knowledge on their respective wards, and will be advised that their leadership on the local implementation may be an example to other staff who were not in attendance *(13.1 Identification of self as a model).* • Post education and training session, the RAPID tool will be available on the wards *(12.5 adding objects to the environment).* Nursing home staff will be prompted to place the RAPID tool in a prominent location (e.g. resident's care plan) to remind staff to complete it every time a resident exhibits behavioural symptoms *(7.1 Prompts/cues, 8.3 Habit formation).* Staff will be encouraged to compete the RAPID tool in conjunction with each other (i.e. nurses and healthcare assistants) with input from GPs, family members and residents, where appropriate *(12.2 Restructuring the social environment).* • The three intervention functions directed at GPs will include: **Education, Environmental Restructuring and Persuasion.** • During the academic detailing session, GPs will be provided with written and oral information regarding the risks and benefits of antipsychotics *(5.1 Information about health consequences)* from a trained academic detailer pharmacist *(9.1 Credible source).* After presenting the evidence, GPs will be asked to consider antipsychotics as the last resort when dealing with the majority of behavioural symptoms, rather than the first-line treatment *(13.2 Framing/re-framing)*, and will be

		encouraged to recommend non-drug alternatives instead of prescribing antipsychotics in these instances *(8.2 Behaviour substitution).* • As part of the academic detailing session, GPs will be introduced to the RAPID assessment tool. However responsibility for its completion will lie with the nursing home staff. GPs will be prompted by staff to review completed RAPID assessment tools when they come to do their ward round, by having them placed in a prominent place (e.g. care plans) *(7.1 Prompts/cues, 12.5 Adding objects to the environment)*. As above, The RAPID tool will focus GPs attention on identifying and exploring patterns of events and triggers that occur in residents (e.g. repetitive actions, sun-downing, pain) *(4.2 Information about antecedents)* that may ultimately lead to an inappropriate prescription of an antipsychotic, and to develop non-drug strategies to use in these situations to address these factors *(1.2 Problem solving).* Nursing home Staff will be encouraged to outline a detailed plan of how and when non-drug and/or drug interventions will be utilised in such situations *(1.4 Action Planning)*, in conjunction with the GP and others *(12.2 Restructuring the social environment).*
WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	1. The education and training sessions: Facilitator will consist of a combination of professions (nursing and pharmacy). Pharmacist facilitators will have at least 3 years post-registration experience as a pharmacist with a postgraduate degree/specialisation in the area of psychotropic medicine use in people with dementia. Nursing facilitators will meet the following criteria: a. At least two year's work experience in supporting people with dementia b. Highly regarded and/or experienced senior care staff, team leader or manager c. Some training or facilitation experience and/or related qualifications d. A degree or postgraduate diploma in dementia or in the relevant area e. Knowledge experience and an understanding of Person-Centred care 2. Academic detailing: Academic detailer will have received 2-day training (by an approved training provider) in conducting academic detailing and will be a pharmacist with at least 3 years post-registration experience with a postgraduate degree/specialisation in the area of psychotropic medicine use in people with dementia 3. Introduction of an assessment tool: The RAPID assessment tool will be introduced by a pharmacist with least 3 years post-registration experience, with a postgraduate degree/specialisation in the area of psychotropic medicine use in people with dementia. The facilitators will be briefed by the research team (if not already part of the research team) and will be provided with the facilitator's manual, slides for presentation to staff and the RAPID assessment tool.
HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as	1. Education and training sessions with nursing home staff (face-to-face, group setting) 2. Academic detailing with GPs (face-to-face, one-to-one) 3. Introduction of an assessment tool (the RAPID assessment tool) to the nursing home environment (face-to-face, group setting)

	internet or telephone) of the intervention and whether it was provided individually or in a group.	
WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	1. Education and training sessions with nursing home staff (off-site, in a local university meeting room) 2. Academic detailing with GPs (in the GP's surgery) 3. Introduction of an assessment tool (the RAPID assessment tool) to the nursing home environment (2 locations; off-site, in a local university meeting room and also on the ward within the nursing home)
WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	1. Education and training sessions with nursing home staff (Once off, Delivered over 14 hours, split over 2 days, two weeks apart) 2. Academic detailing with GPs (Once off, 20 minute session) 3. Introduction of an assessment tool (the RAPID assessment tool) to the nursing home environment (Initially once off (2 hour session) to those in attendance at education and training session. Repeated 1-2 times on each ward to catch different staff, small scale sessions (15 mins each))
TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	N/A
MODIFICATIONS		
10.	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A
HOW WELL		
11.	Planned: If intervention adherence or fidelity was	All facilitators will adhere to a single facilitators guide. All facilitators will meet initially to run through the educational and training sessions at least once beforehand.

	assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	Utilisation of the RAPID assessment tool will be monitored monthly by the research team to assess adherence of nursing home staff to the intervention. Attendance at education and training sessions will also be monitored.
12.	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	Sixteen nursing home staff members attended the two education and training days (seven nurse managers, two staff nurses, five HCAs, one physiotherapist and one occupational therapist). Of approximately 75 staff members working in this nursing home, this represents a 21% attendance rate. All four GPs attending this nursing home participated in the academic detailing sessions (100% attendance rate). Utilisation of the RAPID tool was quite low, and full completion of the tool in adherence with the accompanying instructions was rare. Over the 3 month period, only 19 RAPID tools were utilised – two in full. Of the 12 staff included in the qualitative evaluation that self-reported to have used the RAPID tool, eight acknowledged to have rarely used it (i.e. less than once per week).

Appendix 8. Intervention Materials

See Attached CD-ROM for Intervention Materials for Chapters 6/7.

Appendix 9. RAPID assessment tool

Resident Name (PRINT NAME): _____ Date of Birth: _____

Completed by (PRINT NAME): _____ Date: _____

COMPLETE THIS PAGE ONLY ONCE FOR EVERY RESIDENT WITH A DIAGNOSIS OF DEMENTIA AND KEEP IN RESIDENT'S FILE/FOLDER. THIS PAGE DOES NOT NEED TO BE REPEATED EVERY TIME A RESIDENTS PRESENTS WITH A BEHAVIOUR, UNLESS THE INFORMATION CHANGES OR IF PREVIOUS MEDICAL HISTORY BECOMES AVAILABLE

1. **Does the resident have a confirmed underlying mental health condition (e.g. schizophrenia, bipolar disorder, depression, anxiety disorder?)**
   YES ☐ NO ☐ DON'T KNOW ☐

   If YES, Resident may need psychotropic medication long-term.

   If YES, please specify underlying mental health condition:
   _____

2. **Describe briefly what this resident likes and doesn't like to do.**

Likes	Dislikes

3. **Have antipsychotic medications ever been prescribed for this resident?**
   YES ☐ NO ☐ DON'T KNOW ☐

   If YES and information is available, please list all known antipsychotics that have been prescribed and any additional comments that may be useful (e.g. when it was used, did it work, were there any side effects etc.?)

Antipsychotic(s)	Comments

Full medication history not available for this resident ☐

Resident Name (PRINT NAME): _____ Date of Birth: _____

Completed by (PRINT NAME): _____ Date: _____

COMPLETE PAGES 2-3 EVERYTIME A RESIDENT WITH DEMENTIA PRESENTS WITH A BEHAVIOUR(S). COMPLETE EACH SECTION AS MUCH AS POSSIBLE. NOTE THAT SOME QUESTIONS MAY NOT BE RELEVANT FOR THIS RESIDENT AT THIS TIME.

1. **Describe the behaviour(s) (ABC Charts)**

Date and time	Antecedent	Behaviour	Consequence	Frequency	Severity for the resident
When the behaviour occurred	*What happened right before the behaviour that may have triggered it*	*Describe what the behaviour looked like*	*What happened after the behaviour, or as a result of the behaviour*	*Rare* (< once a week) *Sometimes (once a week)* *Often (several times per week)* *Very often (≥ once per day)*	*Mild (produces little distress)* *Moderate (disturbing but can be redirected)* *Severe (very disturbing and difficult to redirect)*

2. **Circle the resident's behaviour(s). Note that the shaded behaviours are those that are most likely to respond to antipsychotic therapy. Unshaded behaviours are unlikely to respond. *(Circle all that apply)***

BPSD clusters →	**Psychosis**	**Aggression**	**Agitation**	**Depression**	**Mania**	**Apathy**	**Other**
Individual behaviours →	Delusions	Defensive	Restless/ anxious	Anxious	Euphoria	Lack of motivation	Hiding or hoarding
	Hallucinations	Physical	Pacing	Guilty	Irritable	Lacking interest	Wandering without aggression
	Mis-identification	Verbal	Repetitive actions	Hopeless	Pressured speech	Withdrawn	Disinhibition (e.g. sexual)
	Suspicious	Resistance to care	Dressing/ undressing	Irritable/ screaming			
				Sad, tearful			
				Suicidal			

3. **Do any of the behaviours present an immediate risk of harm to self and/or others?**

YES ☐ NO ☐

If YES, Please consider urgent safeguarding measures. Briefly list safeguarding measures utilised: _____

4. **Identify and treat any potential cause(s) of behaviour, or delirium, with input from the resident, healthcare assistants and family (PINCH-ME)**

PINCH-ME	Please tick once assessed	Any action required? Please state.
Pain		
Infection (e.g. urinary tract)		
Nutrition (e.g. hunger)		
Constipation or retention		
Hydration (e.g. thirsty)		
Medications (e.g. anticholinergics)		
Environmental factors		

Additional screening questions for delirium: Yes or No

Is the resident drowsy?

Does the resident have any more difficulty following orders compared to usual?

If the answer to either screening questions is YES, you should consider a formal delirium assessment or medical review

5. **Outline the plan for this resident, with involvement from family (where possible). Non-pharmacological options (e.g. distraction, engagement, adapting the environment) should be attempted <u>first line.</u>**
   Drug therapy may be necessary if the resident poses a risk to self and/or others, multiple non-pharmacological approaches have not worked and reversible causes have been ruled out.

Plan/intervention:

6. **Mutually agree with the GP on a <u>review date</u> for the planned intervention (non-pharmacological and/or drug therapy). Recommend 1-2 weeks when changing dose, 3 months for maintenance. Make a note of the planned review date in resident's drug chart as another reminder.**

Review Date: ___/____/____

Appendix 10. Data Collection Tools for Chapter 7

Resident Data Collection Tool

Date of data extraction				
Year of Birth				
Does this resident have dementia? (Y/N)				
List of ALL psychotropic medicines (Antipsychotics, Antidepressants, Hypnotics/Sedatives, Anti-dementia, Antiepileptics) dispensed from pharmacy in past 28 days (drug, dose, form, frequency)	Drug	Dose	Form	Frequency
PRN administration of psychotropic within last 28 days as indicated on drug chart (drug, dose, form, date and timings of admin)	Drug	Dose	Form	Date and timings of administration
Any changes in psychotropic medicine in last 28 days (drug, dose, frequency, form)	Drug	Dose	Form	Frequency

Number of dose reductions of antipsychotics in past 28 days	
Mean daily dose of antipsychotics (chlorpromazine equivalents)	
FOR RESIDENTS WITH CONFIRMED DEMENTIA DIAGNOSIS ONLY:	
QUM-D Appropriateness score of antipsychotic	
Number of falls in past 28 days	
Total NPI-NH score (from structured survey)	

Pre- and Post-Course Evaluation

1. On a scale of 1-5, how would you rate your understanding of person-centred dementia care?

No Understanding		**Average**	**High understanding**	
1	**2**	**3**	**4**	**5**

2. On a scale of 1-5, how would you rate your understanding of the risks and benefits of antipsychotic prescribing in people with dementia?

No Understanding		**Average**	**High understanding**	
1	**2**	**3**	**4**	**5**

Please indicate your level of agree with the statements listed below

1. The objectives of the training and education were clearly defined.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

2. Participation and interaction were encouraged.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

3. The topics covered were relevant to me, working in a long term care setting.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

4. The content was organised and easy to follow.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

5. The materials distributed were helpful.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

6. This training and education experience will be useful in my work in a long term care setting.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

7. The trainers were knowledgeable about the topics.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

8. The trainers were well prepared.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

9. The training objectives were met.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

10. The time allotted for the training and education was appropriate.

Strongly Agree	*Agree*	*Neutral*	*Disagree*	*Strongly Disagree*
☐	☐	☐	☐	☐

11. What did you like most about this training and education?

12. What aspects of the training and education could be improved, if we were to scale up and deliver it to multiple long term care settings?

13. Have your attitudes towards people with dementia and/or the use of antipsychotics changed since completing this course? If so, please explain.

14. How do you hope to change your practice as a result of this training and education?

15. What do you think worked best, internal facilitation, external facilitation, or a combination? Why?

16. Please share other comments or expand on previous responses here: Thank you for your feedback!

Appendix 11. Topic Guides for Chapter 7

Topic Guide for GPs

So just to start off, what did you think about the project? As I mentioned earlier it included the educational outreach session here and also the RAPID assessment tool in the nursing home
What did you like about it? What did you not like about it? • *[Prompts]* Why/Why not? • *(Ensure discussion covers both content and delivery of education, and the assessment tool)*
In your opinion what impact, if any, did this intervention have? • *[Prompt if not discussed]*
What was the impact on requesting and prescribing of antipsychotics What was the impact on Knowledge, What was the impact on Attitudes, What was the impact on Communication and collaboration with the nursing home staff? What was the impact on the residents and family members? Were there any unintended consequences?
From the educational session, were there any key messages that persuaded you to change your behaviour? *[Prompts] What were those key messages? What did they persuade you to change?*
If nursing staff used the assessment tool with you, how did you find the assessment tool? *[Skip if they say they haven't used it]* *[Prompts] Are there any parts of the assessment tool that are more useful than others?*
Why do you think there was relatively low uptake of the *assessment tool* in the nursing home*?* *[Prompts] How could it be improved? How could it be incorporated into daily clinical practice?*
[You already mentioned a few useful suggestions] Is there anything [else] that could be done differently to make the intervention more beneficial for you? *[Prompts] Are there any components of the intervention that should be dropped or modified? Is there anything missing from the intervention that should be there? (Ensure discussion covers both education, and the assessment tool)*
If this type of intervention is be rolled out to other GP practices, do you have any suggestions to make it better? *(Ensure discussion covers education, and the assessment tool)*
Is there anything else I haven't asked you today that you would like to mention?

Topic Guide for Nursing Home Staff

So just to start off, what did people think about the project? As I mentioned earlier it included the education and training days in UCC and also the RAPID assessment tool.
What did you like about it? What did you not like about it? *[Prompts]* Why/Why not? *(Ensure discussion covers both content and delivery of education/training, and the assessment tool)*
In your opinion what impact, if any, did this intervention have? *[Prompt if not discussed]*
What was the impact on requesting and prescribing of antipsychotics What was the impact on Knowledge, What was the impact on Attitudes, What was the impact on Communication and collaboration with GPs? What was the impact on the residents and family members? What was the impact on the ward as a whole (i.e. were there any knock-on effects to those who didn't attend the education and training days?) Were there any unintended consequences?
[Skip if no-one attended the training days] For those of you who attended the education and training days, were there any key messages that persuaded you to change your behaviour?
How did people find the assessment tool? *[Prompts] Are there any parts of the assessment tool that are more useful than others?*
Why do you think there was relatively low uptake of the *assessment tool?* *[Prompts] How could it be improved? How could it be incorporated into daily clinical practice?*
[You already mentioned a few useful suggestions] Is there anything [else] that could be done differently to make the intervention more beneficial for you? *[Prompts] Are there any components of the intervention that should be dropped or modified? Is there anything missing from the intervention that should be there? (Ensure discussion covers both education/training, and the assessment tool)*
If this type of intervention is be rolled out to other nursing homes, do you have any suggestions to make it better? *(Ensure discussion covers education/training, and the assessment tool)*
Is there anything else I haven't asked you today that you would like to mention?

University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Cork Open Research Archive
Cartlann Taighde Oscailte Chorcaí

Walsh, K. 2019. Rationalising antipsychotic prescribing in dementia: a mixed-methods investigation. PhD Thesis, University College Cork.

Please note that Appendix 12 (pp.412-422) is unavailable due to a restriction requested by the author.

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Appendix 13. Policy Brief

Antipsychotic Prescribing in Nursing Home Residents with Dementia: A Challenging Issue

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Executive Summary:

- Nursing home residents with dementia are commonly prescribed antipsychotics for less than appropriate reasons
- Our synthesis of the literature indicates that nursing homes are using these medicines as a substitute for poor staffing levels and/or inadequate access to services
- Additionally, there is poor understanding of the risks associated with these medicines, with staff often underestimating the harms they can cause (i.e. stroke and death)
- We need to explore ways to tackle these key issues and to help people with dementia live in a restraint-free environment

Introduction:

The number of people with dementia is escalating in Ireland; **estimates project the prevalence at over 147,000 by 2041.**[1] Antipsychotics are commonly used to manage the behavioural symptoms that arise in these patients. **This is especially true in nursing home settings, where approximately 33% of all residents with dementia are prescribed at least one antipsychotic.**[2] However, for a lot of these behaviours, such as wandering and repetitive actions, there is limited evidence that antipsychotics are effective. **Moreover, the evidence points to an increased risk of stroke and death when these agents are used in people with dementia.**[3] Concerns over the use of antipsychotics as chemical restraints have been expressed for many years, however these concerns continue to be raised today.[2]

Why do nursing homes continue to use antipsychotics?

To answer this question, our research team conducted a **systematic review of the qualitative literature.**[4] We then synthesised this evidence in order to gain a deeper insight into this continuing issue. We found 18 qualitative studies, conducted in 6 countries, which explored this matter. None of the studies were conducted in Ireland.

The review discovered several key factors that are influencing prescribers in their decision-making. **One of the key influencing factors is *Organisational Capacity*.** In other words, the capacity of the nursing home to deal with behavioural issues, in terms of staffing and also access to specialist services. In some studies there was a suggestion that antipsychotics were used to compensate for poor staffing levels. Below is a quote from a nurse illustrating this point.

Another key influencing factor is ***Individual Professional Capability.*** Essentially we found that the knowledge and skill level of staff and prescribers had a huge bearing on whether antipsychotics were used as first-line treatment. Some studies concluded that nurses and family members expressed "unfounded high expectations" of the effectiveness of antipsychotics. Other studies concluded that prescribers often lacked adequate knowledge of the risks and benefits of antipsychotics. Below is a quote from a nursing home manager illustrating this point.

Policy Implications:

A key component of our study was a *"Confidence in the Evidence from Reviews of Qualitative research" (CERQual)* assessment. This tool allows researchers and policy-makers to assess the level of confidence in synthesised findings.

Two findings from our review for which we have high confidence in are as follows:

1. Antipsychotics are being used as a substitute for inadequate resources and/or poor access to specialist services

2. More training and education with regards to the management of behavioural issues in dementia is desired

Resources are needed to support nursing homes to deal with behavioural issues in the form of additional staff, and access to non-pharmacological interventions and specialist teams. By providing these supports to nursing homes, this may alleviate some of the pressure on doctors to prescribe antipsychotics.

Training and education should be provided on an ongoing basis to both nursing home staff and prescribers. By educating staff and prescribers on the evidence base and by training staff on how to implement alternative strategies, this could potentially shift the management of behavioural symptoms towards a more holistic, person-centred approach. However, more research is needed to explore ways to tackle these key issues and to help people with dementia live in a restraint-free environment.

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1. Cahill S, Pierce M. *The prevalence of Dementia in Ireland*. Dublin. 2013.
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3. Schneider LS, Dagerman KS, Insel P. *Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials*. Jama. 2005;294(15):1914-1943.
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