Enhancing medicines management in people living with dementia

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This thesis is dedicated to three very special people

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To my nephew Arthur, born sleeping in October 2015

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To my PhD friend Sofina, tragically lost her battles in July 2017

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To my Grandma, who inspired this whole thesis after having dementia herself.

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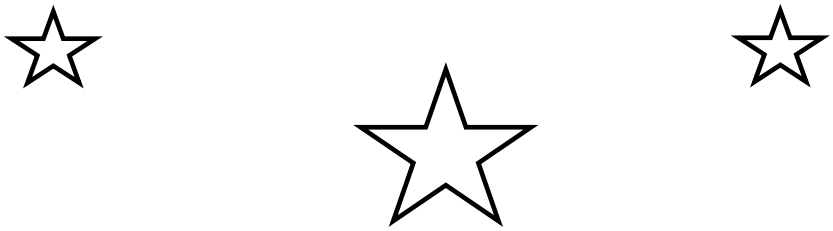

"It does not do well to dwell on dreams and forget to live"
Albus Dumbledore (J.K. Rowling)

I hope this thesis does you all proud.

Abstract

Background: By 2025 there will be over 1 million people living with dementia (PWD) in the UK. Many will develop pneumonia, one of the leading causes of hospitalisation and mortality amongst PWD.

PWD are often prescribed several medicines for a range of health conditions and therefore themselves or their carer need to visit their local community pharmacy regularly. Community pharmacies therefore have the potential to provide greater medicines support to this population.

Aim: This study aimed to develop the evidence base and theory to underpin the development of a community pharmacy intervention which would support people living with dementia within the community.

Methods: Following Medical Research Council guidance for developing an intervention, three studies were conducted to provide elements to be incorporated into a logic model. Firstly, a narrative review of interventions which were targeted at PWD and involved a member of the pharmacy team. Secondly, a case-controlled study using a primary care database to determine the risk factors associated with PWD developing pneumonia. Thirdly, an observational study of PWD living at home to provide a contextualised account of how PWD currently manage their medicines.

Results: The review identified medicine reviews, targeted medicine interventions and memory screening services targeted to PWD which often used a multi-disciplinary team. The case-controlled project showed that dysphagia, chronic obstructive pulmonary disease and liquid formulations were all associated with increased risk of pneumonia in PWD. The observational study showed how the incorporation of medicines into routines is important for effective medicines management.

Conclusion: This study identified that a community pharmacy led intervention could potentially include: Identifying signs of dysphagia, ensuring appropriate formulations are prescribed, exploring the routines of PWD to see how medicines can be better incorporated and using a multidisciplinary team to its best effect. Additional pharmacist training would be required to deliver this.

Keywords: *dementia, community pharmacy, intervention, medicines management*

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List of key abbreviations

ACE Inhibitor	Angiotensin Converting Enzyme Inhibitor
ACh	Acetylcholine
AChEIs	Acetylcholinesterase inhibitors
AD	Alzheimer's Disease
aHR	Adjusted Hazards Ratio
aOR	Adjusted Odds Ratio
AP	Aspiration Pneumonia
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CPRD	Clinical Practice Research Datalink
CVD	Cardiovascular Disease
DAA	Dementia Action Alliance
DSS	Dementia Support Service
ECHO	Economic, Clinical, and Humanistic Outcomes
EPOC	Effective Practice and Organisation of Care
GP	General Practice / General Practitioner
GRADE	Grades of Recommendation, Assessment, Development and Evaluation Working Group
HCP	Healthcare Professional
MDT	Multidisciplinary Team
MMSE	Mini-Mental State Examination
MRC	Medical Research Council
NDD	National Dementia Declaration
NHS	National Health Service
OR	Odds Ratio
PICOS	Population, Intervention, Comparator, Outcome, Setting
PP	Potential Participant
PPI	Proton Pump Inhibitor
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PWD	Person/people living with dementia
RR	Relative Risk
SR	Systematic review
UK	United Kingdom
VD	Vascular Dementia
WHO	World Health Organization

Chapter 1.

Introduction

1.1 Personal and professional context for the PhD

With significant first-hand experience of a grandparent having dementia, I have always been aware of how the disease can affect both the person and the surrounding family. The dementia caused severe memory loss, hallucinations and confusion which caused a great deal of heartache for all of the family but especially for my mother. These memories led me to always be driven to identify approaches to enhance the quality of life of others affected by dementia.

Starting my professional career within community pharmacy, I became acutely aware that even with the growing number of services becoming available in pharmacies, there was limited primary care support targeted to individuals affected by dementia. I saw this lead to medicines not being appropriately managed and people affected by dementia living a lower quality of life.

Both my personal and professional experience has therefore led me to conduct research into how community pharmacy could potentially reach out to people living with dementia (PWD) in the community and help support them.

The rest of this chapter introduces the reader to dementia, medicines associated with dementia, complications associated with dementia, the current role of the community pharmacy and how complex interventions (such as community pharmacy services) are designed.

1.2 Dementia

In order for the medicines management of PWD to be enhanced, it is important to firstly fully understand how many people are affected by dementia, what dementia is and how it progresses with time. This knowledge will be required throughout the research as it will provide insights into why PWD may be prescribed particular medicines and how and why they and their carers manage their daily lives within the community.

The World Health Organisation (WHO) classifies dementia as a syndrome where there is a deterioration in cognitive function beyond what might be expected from the normal ageing process. Several areas of the brain can be affected which may include memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgement. The cognitive impairment found in dementia is also often accompanied by a deterioration in emotional control, social behaviour or motivation [1].

1.3 Prevalence

One in 14 of people in the United Kingdom (UK) who are 65+ years are estimated to have dementia and it has been forecasted that by 2025, the total number of people living with dementia (PWD) in the UK will have increased from approximately 850,000 in 2015 to over 1 million. [2]. Worldwide, there is reported to be approximately 47 million people with dementia which is forecasted to almost triple by 2050 to 132 million [1].

1.4 Types of dementia

There are many types of dementia, which all have different causes and symptoms. Figure 1 presents the prevalence of the most common types of dementia within the UK [3].

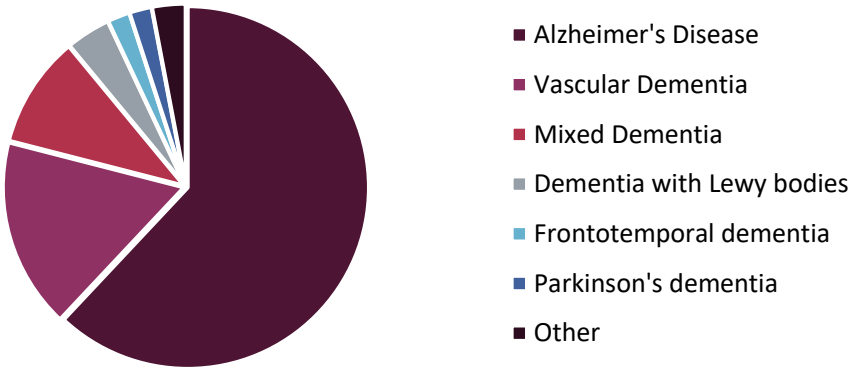

Figure 1. Prevalence of dementia types in the UK

The two most common types, Alzheimer's disease (AD) and Vascular dementia (VD) are discussed in more detail in the following pages.

1.4.1 Alzheimer's disease

The most common type of dementia is AD and is the result of two pathophysiological processes, which together are called the amyloid cascade hypothesis. The first is the accumulation of amyloid-β peptides (AβP) within the brain, which aggregate to produce amyloid plaques and the second is the creation of neurofibrillary tangles from the phosphorylation tau proteins that provide support to the neuron microtubules. Together, the tangles and the amyloid plaques reduce the level of the neurotransmitters acetylcholine, serotonin and glutamate and cause cell death. The resulting brain atrophy (particularly in the grey matter of the cerebral cortex) causes the majority of the signs and symptoms seen in AD [4-6].

AD subtypes

Alzheimer's disease can be divided into two further subtypes, which are typical AD and atypical AD.

Typical AD mostly affects people in their later years (late 70's to 80's) and presents with worsening memory and difficulty in recalling learnt memories due to the hippocampus being the first area of the cortex to be affected. Over several years the cognitive deterioration spreads from the hippocampus to other areas of the cortex.

Atypical AD occurs when the hippocampus is not the first area of the brain to be affected and therefore memory loss is not seen as one of the early symptoms.

1.4.2 Vascular Dementia (VD)

VD affects 17% of the UK dementia population [3] and is generally caused by cerebral vascular disease and ischaemic or haemorrhagic brain injury [7]. Like with atypical AD, the symptoms experienced are dependent on which area of the cortex has been damaged. Symptoms can range from memory impairment, mental slowing, apathy, psychotic phenomena and changes in concentration. Unlike in AD, symptoms can fluctuate throughout the day and can be worse at night. Individuals with VD often have vascular risk factors such as hypertension, smoking, drinking alcohol and a lack of physical activity [8].

1.4.3 Progression of dementia in AD

Figure 2 summarises the three key stages of the progression of typical AD (although the stages often overlap), the percentages of those affected at each stage and the types of interactions and support that may be seen at each stage.

The early stage is commonly overlooked due to such a gradual onset but as the individual enters the middles stages, signs and symptoms become clearer and more restricting. Later stages of dementia often sees nearly full dependence with more serious and obvious signs and symptoms [1, 3]. Additionally, as their condition deteriorates, the interaction and variety of healthcare professionals who are seen increases as various symptoms need managing.

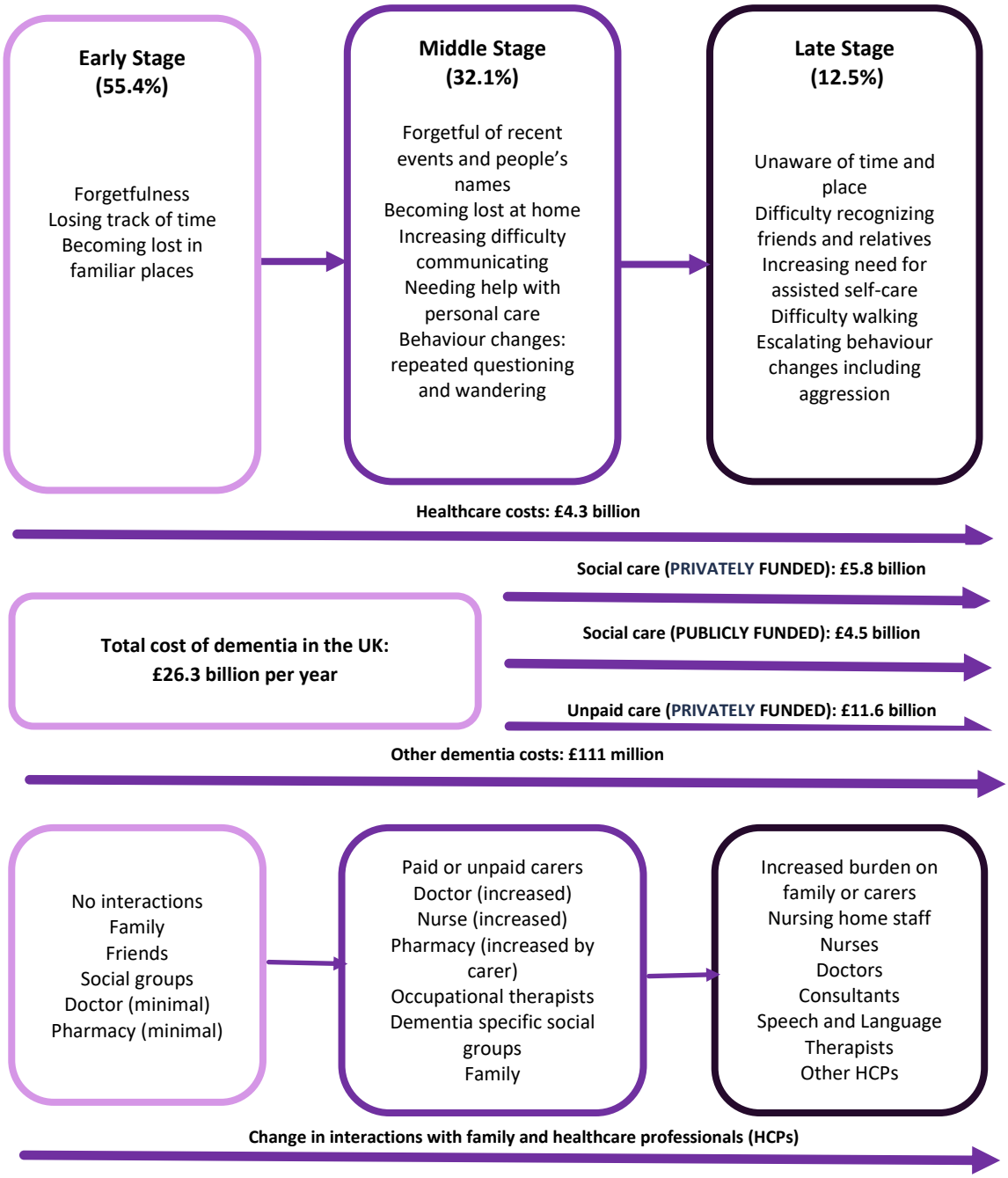

Figure 2. Progression of dementia and associate costs and people interactions

1.5 Medicines prescribed in dementia

All medicines have individual character profiles in regard to their, purpose, efficacy and safety. It is important that researchers designing a medicine-focussed intervention are aware of these, to ensure that any intervention or service is appropriately designed. With this in mind, the following pages introduce medicines commonly prescribed in dementia, which will be useful to be aware of throughout this thesis.

1.5.1 Medicines for dementia

There are two types of medicines available to PWD in the UK, Acetylcholinesterase inhibitors and N-Methyl-D-Aspirate receptor antagonists.

Acetylcholinesterase inhibitors (AChEIs)

In the UK there are three AChEIs licenced for use in mild to moderate AD. Donepezil, Rivastigmine and Galantamine [9]. Figure 3 illustrates how AChEIs block the acetylcholinesterase enzyme on the presynaptic neuron which leads to increased levels of the neurotransmitter acetylcholine within the synaptic cleft. This allows neurotransmission to occur more reliably where neuron cell death and cognitive decline is present (such as in AD).

The resulting increased levels of ACh leads to common side effects such as nausea, vomiting and diarrhoea, which are usually transient and mild in severity and greatly reduced if the dose is titrated appropriately [10, 11].

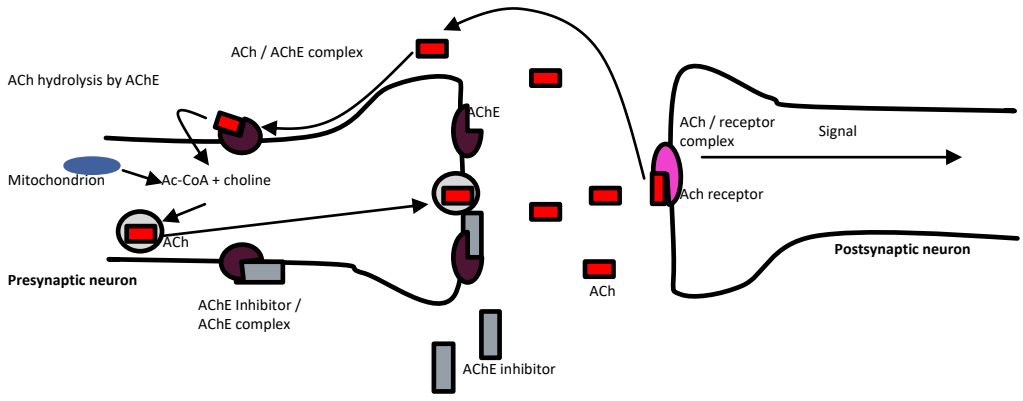

Figure 3. Mechanism of action of AChEIs

N-Methyl-D-Aspirate (NMDA) receptor antagonists (Memantine)

Memantine is licensed in the UK for moderate (where the patient cannot be prescribed an AChEI) and severe AD. Memantine exerts its action by reducing glutamatergic excitoxicity by binding to NMDA receptors. Glutamate is therefore unable to bind and excite these receptors which leads to calcium being unable to enter the ion channel and enter the nerve cells on mass which would otherwise lead to cell death [12, 13].

Clinical effectiveness

The clinical effects reported for both AchEIs and Memantine are negligible. Rainer et al. [14] only reported an improved mean (SD) MMSE score of 11.75 (6.38) at baseline to 13.35 (6.80) at endpoint in an open-label, prospective, 4-month observation study (n=37) of people being prescribed memantine whilst the AD 2000 Collaboration group [15] reported that the Donepezil group averaged 0.8 MMSE points (95% CI: 0.5 to 1.2, $p<0.0001$) higher than a placebo group over the first two years in a UK based randomised, double-blind trial (n=565).

Research and development of new treatments for AD

Due to the limited options currently available to manage AD and their negligible effectiveness, several large pharmaceutical companies are investing in various potential compounds, which use novel mechanisms of action such as beta-site amyloid precursor protein cleaving enzyme (BACE) inhibitors and beta secretase inhibitors [16-19].

These compounds although novel, will not cure dementia but may delay cognition deterioration more effectively than the medicines currently available. However, the development of a new medicine takes a long time and there are no new medicines due to be available to PWD in the near future.

Non-Pharmacological treatments for dementia

With minimal medicines available for PWD, various non-pharmacological treatments have also been explored. Tailored activities which involve naming and counting, exercise, aromatherapy and the use of cognitive stimulation therapy have been identified to potentially aid in the management of patients with dementia and increase their quality of life [20].

A Finnish double-blind randomised controlled trial which was funded by 15 different sources including Alzheimer Association and the Swedish Research Council enrolled 1260

participants who were 60-77 years old into either the intervention group (diet, exercise, cognitive-training and vascular risk monitoring) or the control group (general health advice) between September 2009 and November 2011. Estimated mean change in neuropsychological test battery (NTB) total Z score at 2 years was 0.20 (SE: 0.02, SD 0.51) in the intervention group and 0.16 (SE: 0.01, SD 0.51) in the control group (higher scores suggest better performance). Although these results suggest that cognitive function may be able to be preserved by modifying lifestyle factors, the differences are minimal and the study observed that the most common adverse effect was musculoskeletal pain (5% in the intervention group versus 0% in the control group) possibly due to the exercise [21].

Additionally, Kverno et al. concluded from their systematic literature review (2008) that there is currently a dearth of research in non-pharmacological strategies to treat the neuropsychiatric symptoms of moderate to severe dementia and that more work needs to be done in this area [22].

1.5.2 Other medicines prescribed for PWD

With dementia most often affecting those over the age of 60 and with people living for longer, many PWD will not only be managing their prescribed medicine for dementia but may also be concurrently prescribed other medications for a variety of co-morbidities. Clague et al. calculated in a large cross-sectional study (n=291,169) that PWD are more likely to be to be prescribed five to nine repeat medicines (standardised for age and sex (s) OR: 1.46, 95% CI: 1.40 – 1.52, $p<0.001$) and twice as likely to be prescribed 10 or more repeat medicines (sOR: 2.01, 95% CI: 1.90 – 2.12, $p<0.001$) when compared to those without dementia. The most common conditions that medicines were prescribed in PWD were hypertension (43.2%), constipation (25.9%), coronary heart disease (22.8%), stroke (19.4%) and pain (16.0%) [23]. Lai et al. (n=35,675) also reported that the proportion of polypharmacy (≥5 drugs) was significantly higher in PWD (44.0%) compared to those without dementia (32.0%, $p<0.001$). In PWD, the most commonly prescribed medicines were for cerebrovascular disease (16%), hypertension (16.8%) and chronic kidney disease (12%) [24].

Polypharmacy however increases the likelihood of experiencing an adverse drug reaction (ADR) either due to direct effect of one of the drugs or due to pharmacological interaction between difference drugs [25] and people taking more than three medicines have been

reported to have a 4.3-fold higher risk of an ADR related emergency hospital admission [26].

Although all medicines carry the risk of side effects and adverse events, in PWD, some medicines have greater risks compared to others and, if not taken appropriately, could lead to significant consequences such as reduced quality of life (QOL) or hospitalisation. Medicines identified to carry this greater risk and in need of appropriate prescribing, counselling and administering are detailed below.

NSAIDS

Medicines are commonly prescribed for both acute and long-term pain in the elderly. Some patients may be prescribed non-steroidal anti-inflammatory drugs (NSAIDS) for long periods of time for indications such as osteoarthritis and rheumatoid arthritis but if they are not administered appropriately (such as without food or a concurrent proton pump inhibitor (PPI)), they are known to increase the risk of gastrointestinal bleeding and possibly cardiovascular events in elderly populations [27, 28].

Opioids

Opioids may be prescribed for more severe pain which can cause sedation and confusion which could lead to falls and hospitalisation [29]. Opioids also commonly cause constipation, which then requires the prescribing of a laxative to counteract these side effects which leads to increased pill-burden to the PWD.

Anti-depressants

It has been documented that roughly 50% of patients with dementia will suffer with depression at some stage in their disease and in some cases, it may even be an early symptom of undiagnosed dementia [30]. Dementia and depression has a complex relationship with evidence to support both early-life depression being associated with an increased risk of dementia and late-life depression being a pro-drome of dementia [31].

Many PWD may be prescribed a selective serotonin re-uptake inhibitors (SNRI) or a tricyclic antidepressant (TCA).

TCA's possess varying degrees of anticholinergic properties, which means that if TCA's are co-prescribed in PWD, they may enhance the degenerative process by further reducing ACh levels. This could lead to enhanced dementia symptoms such as increased confusion or enhanced anticholinergic side effects such as dry mouth, blurred vision and constipation,

which may require further medicines to be prescribed. Antidepressants (along with other anticholinergics such cyclizine, prochlorperazine and oxybutynin) should therefore be prescribed mindfully and with caution in PWD [32].

Anti-psychotics

PWD can experience episodes of behavioural and psychological symptoms of dementia (BPSD) which includes agitation, hallucinations, delirium and aggressive behaviour [33]. To control these symptoms, antipsychotics (usually the newer atypical medicines such as risperidone, olanzapine and quetiapine) are frequently prescribed. These antipsychotics (except for risperidone) are prescribed "off-label", meaning they are not licensed to be prescribed for BPSD. In the UK, risperidone is the only antipsychotic licensed to be used in moderate to severe Alzheimer's dementia for persistent aggression where non-pharmacological approaches have not been successful and where there is risk of harm to self or others. However, it is only licensed for short-term use (i.e. for a maximum of 6 weeks). Antipsychotics have anticholinergic properties which means that they are essentially doing the opposite of AChEIs and memantine which work by increasing levels of ACh. This means that they can counteract any benefits seen by the dementia medicines and lead to an increased deterioration of the disease or cause increased anticholinergic side effects such as confusion, drowsiness, dizziness, hallucinations, constipation and blurred vision.

Sometimes antipsychotics can be unnecessarily prescribed in PWD. An estimated 50% of PWD across the world experience regular pain yet their cognitive decline can make it more difficult to self-report their pain and for pain to be adequately managed, as often the distress and behavioural difficulties shown by PWD unable to communicate their pain can be misdiagnosed for psychological issues [34].

In 2009, the Banerjee report estimated that there were 180,000 people with dementia prescribed antipsychotic drugs but were only having a beneficial effect in roughly one third of cases. Further to this, it was estimated that there would be 1,620 cardiovascular adverse events and 1800 deaths occurring annually as a result of antipsychotic use [35]. Since this report, there has been an increased emphasis on improving the care to patients with dementia including the reduction in prescribed antipsychotics.

1.6 Complications of dementia

As dementia progresses and the condition becomes more severe, complications such as dysphagia and the risk of contracting pneumonia may occur.

1.6.1 Dysphagia

Jeri Logemann [36] defines dysphagia as 'a difficulty moving food from mouth to stomach'. Signs that a patient is experiencing dysphagia may typically include: clamping the mouth shut; dribbling food out of the mouth; pooling the food in the mouth; delayed swallowing; the slumping of the head and shoulders; eating more slowly and refusing to eat or drink.

There are various causes that may lead to a PWD experiencing problems with their swallowing which include [37]:

Prescribed medicines

Central nervous system medicines

Medicines that act as central nervous system (CNS) depressants such as sedatives, antipsychotics, anticholinergics and barbiturates can impair a person's consciousness and cause slower swallowing reflexes. They can also cause further confusion leading to the person finding the swallowing process confusing.

Additionally, the extrapyramidal symptoms associated with antipsychotics can affect the swallowing process. Often, medicine induced dysphagia instances can be reversed over several months once the medicine is stopped.

Medicines that cause oesophageal disorders

The coating on the formulation, the size of the formulation or the pH of the formulation can all cause injuries to the oesophagus [38, 39] and are exacerbated by factors such as: fasting, poor posture when swallowing the medicine, reduced saliva, inadequate volume of fluid taken alongside the medicine, duration of direct contact between the drug and the mucosa, age, and polypharmacy.

Medicines that affect salivary flow

Tricyclic antidepressants, anti-parkinsonian medicines, diuretics, antipsychotics, anti-hypertensives and antihistamines can all reduce salivary flow and cause xerostomia. This can lead to poor oral hygiene and a favourable environment for pathogens, which may initiate further complications such as pneumonia.

Age

As dementia mostly affects older people, some PWD may experience symptoms of dysphagia due to an ageing anatomy. Symptoms include:

- Reduces sense of smell and taste [40]
- Loss of teeth [41]
- Reduced muscle reflexes in the mouth and throat and the entering of residue into the lungs leading to eating taking longer and increased coughing [42]
- Decreased tissue strength. Lower hanging tongue, reduced tongue pressure and reduced lip function [43]
- Shrinkage of gums and dentures becoming ill-fitting [44]

Cognitive function decline

The reduced cognitive function in dementia can lead an inability to recognise food as food (agnosia). PWD may therefore be hesitant to place the food in their mouths or may be confused as to what they are meant to do next once the food is successfully in the mouth.

The inability to perform tasks that a person is mentally willing to do (apraxia) may also develop in the later stages of dementia which can cause utensil use and the initial oral stages of feeding difficult.

A loss of smell (anosmia) due to a loss of olfactory senses and damage to the olfactory bulb in dementia can further cause swallowing related difficulties as a lack of taste, reduced saliva production and loss of appetite can be seen. Foods may then need additional seasoning or sugar added which can have a negative effect on their health.

Horner et al. [45] reported that the most common swallowing problems in AD were a delayed gag reflex, prolonged oral phase and inefficient clearance of substances into the oesophagus.

Vascular dementia

Where brain damage has occurred (such as in VD), there may be separations between the neural pathways between the cortex (where the oral stages of the swallow are controlled) and the medulla (where the pharyngeal stage of the swallow are controlled). This means that a PWD may initiate a swallow by command but the pharyngeal swallow is not triggered [36].

1.6.2 Pneumonia

A nested case-control study (2006) funded by the Health Protection Agency used primary care data from 443 general practices in the UK. The study included 17,172 cases of pneumonia and 71,399 controls and estimated that PWD were 2.45 (95% CI: 2.13 to 2.81) times more likely to develop pneumonia compared to a population who did not have dementia [46].

Aspiration pneumonia (AP)

AP is a particular form of pneumonia which occurs when a person aspirates and transfers pneumonia causing pathogens into the lungs. Aspiration is very common in dysphagic patients. A Spanish prospective cohort study (January 2001 – August 2005), which included 1-year follow-up and based in an acute geriatric unit (n=134) observed 74 (55.2%) participants who were consecutively admitted with pneumonia to have oropharyngeal dysphagia and aspiration present and of the participants with dementia, 37 (82%) had dysphagia [47].

A narrative review of current literature identified 7 studies that assessed the incidence of pneumonia in stroke patients with dysphagia to range from 16-33%. However, the range of incidence seemed dependant on the type of study population (acute or rehabilitation) and the baseline incidence. Pooled analysis generated relative risk (RR) scores of 3.17 (95% CI; 2.07, 4.87) for risk of pneumonia in dysphagia compared to those without dysphagia and an even higher RR score of 11.56 (95% CI; 3.36, 39.77) for patients with confirmed aspiration compared to those without.

The study therefore concludes that there was a 3-fold increase in pneumonia risk among stroke patients with dysphagia and an 11-fold increase in risk among a subset of patients with confirmed aspiration pneumonia. [48].

Pneumonia protective factors

Proposed protective factors for pneumonia in PWD have been identified. A Canadian prospective cohort study by Loeb et al. [49] observed 475 nursing home residents from 5 metropolitan Toronto, Ontario nursing homes between July 1993 and June 1996. The study reported that receiving the influenza vaccination was a protective factor against developing pneumonia (OR: 0.4, 95% CI: 0.3 - 0.5, p=0.01). Furthermore, a prospective observational multicentre study from the United States and funded by the Influenza Division in the National Centre for Immunisation and Respiratory Diseases at the Centres for Disease

Control and Prevention (n=2,767) determined that the adjusted OR for developing pneumonia after receiving an influenza vaccination was 0.43 (95% CI: 0.28 – 0.68) [50]. This association is logical as in many cases, pneumonia often develops as a secondary complication to the influenza [51].

The use of the pneumococcal vaccination should also logically reduce the risk of pneumonia, but two Japanese studies have found marginal effectiveness in elderly populations. Kondo et al. [52] conducted a case-control study supported by Health and Labour Science Research Grants in the period of October 2009 to September 2014. The study comprised of 672 outpatients from 24 hospitals in Tokyo and reported an OR of just 0.59 (95% CI: 0.34 – 1.03). Suzuki et al. [53] reported a 27.4% (95% CI: 3.2 – 45.6) effectiveness against all pneumococcal pneumonia and 2.0% (95% CI: -78.9 – 46.3) against non- pneumonia vaccination serotypes in a multicentre, prospective study which included 2036 individuals aged 65 years or older with community -acquired pneumonia who visited four study hospitals in Japan between September 2011 and August 2014..

Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) have also been reported to have protective properties against pneumonia. A population based, retrospective cohort study conducted in Ontario, Canada reported how patients who had filled a prescription for ACEs and ARBs had reduced risks of hospitalisations for pneumonia with respective adjusted relative risks of 0.61 (95% CI: 0.46 – 0.81) and 0.52 (95% CI: 0.36 – 0.76). The study used five linked databases of health administrative data from June 2003 and December 2011 and included 254,485 patients [54].

Bosch et al. [55] prospectively evaluated elderly patients from Spain with dementia who had been hospitalised due to AP in 2010. 28.3% experienced repeat episodes of AP and these patients were less frequently prescribed ACE inhibitors (8.8% vs 27.9%; $p<0.001$) when compared to patients presenting with their first episode of AP. The authors hypothesised that the protective effect also observed in their study against AP may be due to the ACE inhibitors increasing levels of substance P by inhibiting its breakdown. Substance P is used in the swallowing and cough sensory pathways and so if levels are increased it may improve symptomless dysphagia.

However, Dublin et al. [56] actively minimised detection bias and selection bias by using a 2:1 ratio in a USA based nested case-control study (n=3061) of community-dwelling, immunocompetent adults aged 65-94. Cases of ambulatory and hospitalised pneumonia were identified between the years of 2000 – 2003 and were matched to controls on age,

sex and calendar year. The study concluded that ACE inhibitor use was not associated with reduced pneumonia risk in community-dwelling patients (OR: 0.99, 95% CI: 0.83 - 1.19).

Risk factors for pneumonia

There have been many risk factors identified within the literature which have been associated with developing pneumonia, particularly in elderly cohorts. In the following few pages, these risk factors (which could be relatable to PWD) are introduced along with the associated evidence.

Proton Pump Inhibitors (PPIs) and histamine$_2$ receptor antagonists (HRAs)

Ho et al. conducted a retrospective population-based cohort study, which sourced data from registration and claims data in Taiwan from 2009 – 2013. The study consisted of 1,572 patients aged ≥40 years with new-onset dementia and it was calculated that the incidence of pneumonia was higher amongst patients with PPI usage compared to those without (adjusted hazard ratio: 1.89, 95% CI: 1.51 – 2.37, p<0.01) [57]. The study matched patients on numerous comorbidities such as dysphagia and hypertension in addition to some medicines such as antipsychotics which were potential confounders which made the results more believable. Limitations to this study included the 1:1 matching which gave the study less statistical power (in comparison to a study where there is 3:1 or 4:1 matching) and the reliance of a database which is subject to human input error and limited information such as the severity of the dementia and medication compliance. There was also no inclusion of smoking or dental hygiene which were other potential confounders.

Building on the above research, a study which combined a meta-analysis and systematic review of 8 observational studies (5 case controls and 3 cohort studies) and 31 RCTs reported that subjects prescribed PPIs or HRAs had a higher overall risk of developing pneumonia (aOR: 1.27, 95% CI: 1.11 - 1.46, Higgins I^2 value: 90.5%), (aOR: 1.22, 95% CI: 1.09 - 1.36, I^2: 0.0%) respectively. The 23 RCTs reviewed showed the risk of pneumonia appearing greater in low-quality studies (RR: 1.35, 95% CI: 1.10 - 1.67, I^2: 12.5%) when compared to the higher quality studies which had no effect (RR: 0.96, 95% CI 0.65 - 1.43, I^2: 47.0%) [58]. This study used validated methods such as the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) and conducted a thorough analysis (additionally looked at several sub-groups. However, there is the possibility that not all of the studies considered the potential confounder, gastroesophageal reflux disease, which in

itself could be a risk factor for pneumonia and could have introduced some slight bias into the results. Although the higher quality RCTs showed no effect, overall, the results from this study are suggestive of there being an association.

Smoking

A large prospective cohort study from the US (n= 104,491) compared never smokers to current smokers and reported that current smokers were associated with an increased risk of community acquired pneumonia (CAP) amongst both men (RR: 1.46, 95% CI: 1.00 - 2.14) and women (RR: 1.55, 95% CI: 1.15 - 2.10) [59]. This study had a 6 year follow up for men and 2 year follow up for women and gathered data by using questionnaires. This method would have been open to recall bias as the participants were asked to self-report if they had had pneumonia. The researchers aimed to minimise this however by reviewing the medical notes of all the men and a random sample of 76 women. The large sample size in this study and the fact that possible confounders were considered and excluded from the study makes the results worthy of further consideration.

Tobacco smoke (including passive exposure) has also been identified as the most important causative factor in the development of COPD [60] as it can cause a number of changes such as the airway epithelium changing to protect the lung from the smoke and inflammatory response [61]. A US based, cross sectional study by Cunningham et al. used data from the 2011 Behavioural Risk Factor Surveillance System and included 405,856 adults aged 18 years or older. It was determined that the likelihood of current smokers having COPD was almost four times higher (prevalence ratio: 3.9%, 95% CI: 3.7 – 4.1) compared to never smokers [62]. This supports the theory described by Cunha et al. [63] that smoking is associated with developing COPD such as chronic bronchitis which in turn, may predispose the person to pneumonia.

Co-morbidity

The 2006 UK based nested case-control study which was described at the beginning of this section (Section 1.6.2) (number of cases= 17,172) [46] reported that many co-morbidities were associated with an increased risk of CAP including:

- Heart disease (aOR: 1.63, 95% CI: 1.54 – 1.72)

- Respiratory disease (aOR: 2.42, 95% CI: 2.31 – 2.53
- Osteoporosis (aOR: 1.57, 95% CI: 1.41 – 1.74)
- Diabetes (aOR: 1.36, 95% CI: 1.27 – 1.47)
- Rheumatoid arthritis (aOR: 1.84, 95% CI: 1.62 – 2.10)

Although this study had a few limitations due to the data source (a primary care database) such as limited and inconsistent information for potential residual confounders, the main confounders are included in the study and limited bias will have been created.

In addition to his results regarding PPIs, Ho et al. [57] reported an association between a number of comorbidities and an increased risk of developing pneumonia:

- Underlying cerebrovascular disease (aHR: 1.30, 95% CI: 1.04–1.62)
- Chronic pulmonary disease (aHR: 1.39, 95% CI: 1.09–1.76)
- Congestive heart failure (aHR: 1.54, 95% CI: 1.11–2.13)
- Diabetes mellitus (aHR: 1.54, 95% CI: 1.22–1.95)

Inhaler devices and inhaled steroids for COPD and asthma

A Spanish population-based, case-control study (November 1999- November 2000) of individuals over 14 years of age (n= 1,336 [case], 1,326 [control]) reported how the use of inhalers with or without a spacer (used in COPD and asthma) may be independently associated with a 1.57 (95% CI: 1.04 – 2.38, p=0.031) chance of developing CAP which they explain may be due to poor hygienic measures and contamination of the inhaler/spacer and deep inhalation aiding the penetration of microorganisms into the bronchial tree [64].Although the authors speculate to what the underlying causes for the reported association may be, due to the observational nature of this study, there may be other confounding factors which have not been considered.

A systematic review conducted in 2013 of 43 parallel-group RCTs of at least 12 weeks duration [65] reported that inhaled fluticasone (also used in asthma and COPD) was associated with an increased risk of developing non-fatal, serious adverse pneumonia events (OR 1.78, 95% CI 1.50 – 2.12) and budesonide increasing the likelihood by 1.62 (95% CI 1.0 – 2.62).

Residence

A Spanish prospective, population-based cohort study (n= 27,204) estimated that patients residing in nursing homes were associated with an increased risk of developing pneumococcal pneumonia (Hazards ratio: 4.59, 95% CI: 2.32 – 9.11, p<0.001) [66]. This was a relatively large study which adjusted for possible confounders such as smoking. The methods used for identifying incidences of pneumonia however meant that there may have been an under-identification of some events (of pneumonia), which in turn may have led to the relatively low number of case events that were available for analysis. The low numbers of events are reflected in the wide confidence intervals seen for some of the characteristics.

Gender

Ho et al. (previously described for PPIs), calculated that male gender was associated with a higher risk (aHR: 1.57, 95% CI: 1.25 - 1.98) of developing pneumonia [57].

The Canadian prospective cohort study (n=475) by Loeb et al. (described earlier in this section under 'pneumonia protective factors') found similar findings with males being associated with almost double the likelihood of developing pneumonia (OR: 1.9, 95% CI: 1.1 - 3.5, p=0.03) [49]. Although the results from this study are in line with Ho et al. [57] this was a very small study with a high attrition rate over the 3 years (n= 79 by year 3).

Oral Health

A US based cohort study which involved the prospective enrolment of veterans aged 55 years and older who were outpatients, inpatients or residents of the nursing home of the Ann Arbor Medical Centre. The study ran from 1990 to 1998 and involved retrospective analysis. The study (n= 358) observed a variety of oral health factors in a sub-group of dentate patients (n=220) which were associated with developing AP and the results are reported in Table 1 [67].

Table 1. Oral health characteristics associated with aspiration pneumonia

Characteristic	Odds Ratio	95% Confidence Interval
Needing help feeding	13.9	3.2 – 60.8
Porphyromonus gingivalis	4.2	1.6 – 11.3
Streptococcus sobrinus	6.2	1.4 – 27.5
Staphylococcus aureus	7.4	1.8 – 30.5
Number of decayed teeth*	1.2	1.1 – 1.4
Number of functional dental units	1.2	1.02 – 1.4
**For each additional decayed tooth*		

This study used objective measures to determine a diagnosis of pneumonia and many of the characteristics reported and had a long follow-up of 9 years.

The association of AP and oral health has however been reported in another more recent study. Naruishi et al. [68] conducted a cross-sectional study of 1174 elderly patients who had been admitted to one of two Japanese hospitals between 2012 and 2016. and reported that the incidence of AP was higher in patients with both cognitive impairment *and* the loss of posterior occlusion (OR: 4.50, 95% CI: 3.4 – 5.9) compared to only having either factor alone. Nurses evaluated nutritional status and dentists evaluated the oral condition of participants and were blinded to background information and used objective, validated methods such as the clinical dementia rating scale.

Tube Feeding

Cintra et al. [69] conducted an observational, prospective, non-randomised and unblinded study between July 2011 and September 2012. The study included 67 patients from health facilities in Brazil who had possible or probable AD, moderate to severe oropharyngeal dysphagia and aged over 60 years of age. The study reported that the relative risk of developing AP in patients with advanced AD and oropharyngeal dysphagia who were receiving alternative feeding (such as nasogastric tube) was 2.32 (95% CI: 1.22 – 4.40) compared to those feeding orally.

Oral medicine formulations

The 3-year, Canadian multiple centre cohort study by Loeb at al. (n=254), previously mentioned and described regarding gender and influenza vaccinations reported that nursing home residents who were having their first episode of pneumonia were eight times more likely to be unable to take oral medication (aOR: 8.3, 95% CI: 1.4-50.3) [49].

Antipsychotics

A small study (n=121) based in two Japanese psychiatric hospitals (year unknown) retrospectively reviewed clinical records of 104 AD patients for the potential risk factors of aspiration pneumonia and examined the swallowing reflex of 17 other patients with AD before and after the intake of either a neuroleptic or a benzodiazepine. Aspiration pneumonia was reported to be significantly and independently associated with neuroleptic dose (OR: 3.13, 95% CI: 1.46 - 6.69, p=0.003) and neuroleptics were additionally reported to significantly lengthen the swallow reflex latency (SD) from 2.0 seconds (0.6) to 7.7 seconds (2.6) ($p<0.05$) [70].

A nested case-control study from the Netherlands [71] used data from a database which collates information from community pharmacies and hospital discharge records to investigate the association between antipsychotic drug use and risk of pneumonia in elderly people. The study identified 22,944 people aged 65 and older with at least one antipsychotic prescription from April 1985 and December 2003 and randomly matched four controls by index date to each of the 543 cases who had a hospital admission for pneumonia. The study reported that current use of antipsychotics were associated with a 60% greater risk of pneumonia (aOR: 1.6, 95% CI: 1.3 – 2.1). Antipsychotic duration of use was also found to have an inverse relationship with pneumonia risk with risk being highest during the first week after initiation (aOR: 4.5, 95% CI: 2.8 – 7.3). Authors suggested several possible reasons for the association of antipsychotic use and pneumonia:

- The blocking of dopamine receptors by the antipsychotics leads to rigidity and spasm of the oropharyngeal muscles resulting in aspiration.
- Antipsychotics can cause xerostomia (dry mouth) due to the high anticholinergic activity seen in some of them which can lead to impaired bolus transport which may result in aspiration.
- Antipsychotics can cause drowsiness by blocking the histamine-1-receptor in the central nervous system which can lead to swallowing problems and aspiration.

This study used 4:1 matching to increase power and took into consideration a number of confounders such as diabetes mellitus, heart failure, benzodiazepines and gastric acid suppressive drugs. One of the main limitations to this study is the reliance of data input and possibility for human error. Only pneumonia which resulted in hospitalisations were identified and they required a definite diagnosis within the notes. Both of these factors

open the study up for potential under-reporting of pneumonia. The results from this study do suggest an association worthy of further investigation in a dementia specific cohort.

A case-control study [72] (n= 208) observed between February 1997 and January 1998 that residents of a veterans affairs long-term care facility in Pittsburgh, USA who had been prescribed tranquilizers in the 14 days before pneumonia onset, were more likely to develop pneumonia (OR: 2.6, 95% CI: 1.2-5.4, p=0.01).

Hospitalisation

Rudolph et al. [73] conducted a prospective cohort study which followed community dwelling patients with AD from the Massachusetts Alzheimer's Disease Research Centre based in the US. Participants were enrolled between January 1991 and June 2006 and consisted of individuals aged 65 and older with a clinical diagnosis of possible or probable AD. The study (n=542) reported that pneumonia (6%) was the fourth most common cause of patient with AD being admitted to hospital behind gastro-intestinal disease (9%), ischemic heart disease (17%) and syncope, fall or trauma (26%). The author hypothesises that people with early stage AD may be more likely to be hospitalised compared to age-matched peers due to their cognitive decline causing judgement errors, medication errors or non-adherence.

Voisin et al. [74] aimed to evaluate the frequency and causes of hospitalisation in a large (n=686) prospective cohort of mild to moderate AD in France between 2000 and 2002 in 16 participating centres. The annual incidence of hospitalisation was 26.1% (95% CI 22.5 - 29.7) with the number (%) being admitted once, twice, thrice and four times during the 2 years being 139 (68.8), 40 (19.8), 17 (8.4) and 4 (2) respectively. The principal causes were; cardiovascular disorders (14.5%), fractures (12.7%), behavioural disorders (11%) and infectious disease (including pneumonia) (3.9%). Hospitalised patients with AD had a length of stay 14.3 ± 23.5 days.

This study highlights the high hospitalisation rate in patients with mild-moderate AD and that pneumonia is potentially one of the most common causes.

An older study retrospectively reviewed the medical records of 81 patients with dementia who transferred from a skilled, long-term care nursing facility based in New York to a local hospital for acute hospital care between 1982 and 1985 to ascertaining the frequency and cause of acute hospitalisation of PWD in a long term care facility [75]. It was reported that

34.2% of acute admissions were due to respiratory disorders of which 46 of these 75 patients had pneumonia. The authors conclude that PWD may be more prone to acquiring life-threatening infections and that facilities that care for this population should ensure that extensive preventative programmes are in place to reduce acute hospitalisation and reduce health costs.

Consequences of hospitalisation

When PWD are admitted to hospital, they can become disorientated from the different and often not dementia friendly surroundings. This can lead to delirium and a PWD declining more rapidly, increasing their chances of further hospitalisations and mortality, increased reliance on care givers, depression, increased likelihood of falls and an increased reliance on care givers [76, 77].

Furthermore, not only are the PWD affected from being admitted to hospital, but carers have also reported 'physical and emotional exhaustion, regardless of the quality of care received in hospital' [78].

Some PWD who are admitted may develop further complications in addition to a decline in their cognitive function which may mean that they require increased nursing care and are moved into a nursing home. A retrospective cohort study 16,186 participants aged 65 years or older who were part of an ongoing longitudinal study, the Health and Retirement Study (HRS), based in the US, calculated participant's transitions of care between home, home with formal services, hospital and nursing facilities between 1999 and 2008 using HRS and Medicare claims data. From the 8,433 transitions which were made exclusively by PWD, it was calculated that 52.2% transitioned back home with no formal services, 6.9% transitioned back home with formal services and 33.8% transitioned to a nursing facility. The authors concluded how it is necessary to improve support at home and in nursing homes as we prepare for growing numbers of individuals with dementia transitioning across settings with increasing levels of acute and chronic care needs [79]. This study reinforces how a growing number of PWD are residing in the community and therefore the need for improved support at a community level for PWD and carers of PWD. The study also highlights how a third of PWD who were hospitalised deteriorated during their stay which led to a transition to a nursing home. This shows the effect that hospitalisation can have on PWD and reinforces how more measures are needed to help prevent PWD being hospitalised in the first place.

Mortality

Several studies have identified pneumonia as a major cause of death in PWD. Todd et al. [80] reviewed the death certificates of 85 people with AD and compared against a control group (n=52) which consisted of the general population. Pneumonia was calculated to cause significant excess deaths in the AD group compared to the general population (standardised mortality rate: 259, 95% CI: 145 – 427). Additionally, although pneumonia was the second most common underlying cause of death in the controls (25%) after cardiovascular disease (28.8%), pneumonia was also the second most common underlying cause in those with AD (17.6%) after AD (itself 23.5%). Authors concluded that pneumonia contributes to mortality to a higher extent compared to other causes in patients with AD and in comparisons to those without AD.

Brunnström et al. [81] studied the reports of 524 autopsies on PWD and found that the most common causes of death were bronchopneumonia (38.4%) and ischaemic heart disease (IHD) (23.1%). For comparison, reports were also studied of a general population where bronchopneumonia accounted for just 2.8% and IHD was 22.0%. The authors reason that this common immediate cause of death could be a reflection of the terminal stage of the dementia where patient care and feeding can become difficult.

Burns et al. supports these results as bronchopneumonia was recorded as the most common cause of death in people with AD at post mortem in addition to on death certificates [82].

1.6.3 Section Summary

In summary, dementia can be the start of a sequence of severe consequences. People living with severe dementia are likely to develop dysphagia which may in turn lead to aspiration pneumonia and consequently hospitalization, which in turn may lead to a deterioration in the condition and lead to either death or transfer to a nursing home.

However, if the individual does not develop dysphagia, this section has highlighted a number of other potential risk factors such as antipsychotics and co-morbidities such as COPD and diabetes for developing pneumonia and potentially leading to hospitalisation and a deterioration in the dementia.

1.7 The National Dementia Declaration

In 2009 a 5-year national dementia strategy was published and the creation of the Dementia Action Alliance (DAA) followed in 2010. The DAA brings together over 600 organisations from various sectors to promote their aim [83]:

> *"To transform the lives of people with dementia and those that care for them through building commitment and actions to deliver the National Dementia Declaration (NDD)"*

The NDD was created by people affected by dementia along with organisations who seek change. The NDD consists of the following 7 outcomes that people affected by dementia have described to be important to them and would like to see in their lives [84]:

1. I have personal choice and control or influence over decisions about me
2. I know that services are designed around me and my needs
3. I have support that helps me live my life
4. I have the knowledge and know-how to get what I need
5. I live in an enabling and supportive environment where I feel valued and understood
6. I have a sense of belonging and of being a valued part of family, community and civic life
7. I know there is research going on which delivers a better life for me now and hope for the future

1.8 Support networks for PWD

Many PWD living in the community will also be living with a spouse or family member who will be acting as their informal carer. This means that, dependent on the stage of the dementia, they may be responsible for washing and feeding the PWD, or may simply help remind the PWD to take or collect their medicines. Carers (both informal and formal) however often lack training in medicine administration, possess minimal knowledge about the medicines and have little understanding of how to communicate effectively with a patient with dementia that may then lead to sub-optimal medicine management [85].

A literature review by Wills and Soliman [86] describes how a carer's physical and emotional health can suffer when they are caring for someone living with dementia, particularly in regards to the levels of stress and perceived burden. A cross-sectional study published in 1998 used clinically valid scales and self-report questionnaires to explore the impact of subgroups and individual symptoms of non-cognitive disturbance on the carers of

patients with AD. The study included 100 patients with AD living at home and their carers, who used the Old Age Psychiatry Outreach Services in South and Central Manchester. The study found that the non-cognitive features of AD such as mood and behavioural signs of depression in the PWD were the most stressful for carers [87].

In 1996, Livingston et al. [88] conducted a study in the London Borough of Islington, which consisted of interviews (in the way of a validated semi-structured questionnaires and revised clinical interview schedules) at the homes of 760 subjects and co-residents (of which 118 were subject's informal carers) to assess psychiatric morbidity and physical disability. The study found that within the 64 women carers, there was a higher risk of depression in the carers of PWD (47%, 95% CI: 21.42 – 71.91) when compared to women co-residents ($p<0.05$) and was more commonly found compared to women carers of people with depression (13%, 95% CI: 0.00 – 30.54), other psychiatric illnesses (30%, 95% CI: 13.60 – 46.40) or those caring for relatives with a physical disability (3%, 95% CI: 0.00 – 8.62).

The newly published NICE guidelines (2018) [77] provides specific guidance on how carers should be supported which includes:

- Develop personalised strategies and build carer skills
- Training to provide care and adapt their communication styles
- Advice on how to look after their own physical mental health, emotional and spiritual wellbeing
- Information about relevant services (including support services) and how to access them
- Ensure the support provided to the carers is:
    - Tailored to their needs
    - Designed to help them support PWD
    - Available at a location they can get to easily
- HCPs being aware that carers of PWD are at an increased risk of depression

The PWD and/ or carer may find it difficult to access support from their GP or another HCP whereas the community pharmacist, they may already be visiting on a regular basis to collect their repeat medicines.

This consistent visit to their local pharmacy therefore provides an opportunity for the community pharmacist to provide further support to the patient in a variety of ways as the pharmacist role moves from a dispensing role to a more clinical, patient focussed role [89].

1.9 Community Pharmacy role

Community pharmacies in the UK are able to conduct a wide range of services, which are categorised into Essential Services, Locally Commissioned Services and Advanced Services. This section provides a brief introduction into these services as it will help to provide context as to how community pharmacy could greater support PWD in the way of a new intervention.

Essential Services are services which are offered by all pharmacies as part of the NHS Community Pharmacy Contractual Framework and include the dispensing of medicines, repeat dispensing, disposal of unwanted medicines and signposting.

Locally Commissioned (LC) Services (previously called Enhanced Services) are services which can be contracted by different commissioners such as the local authorities, clinical commissioning groups (CCGs) and local NHS England teams. Locally commissioned services found in some pharmacies include Healthy Living Pharmacies, chlamydia screening and treatment, smoking cessation, Emergency Hormonal Contraception, Minor Ailment Service, Needle and Syringe Programmes and Vaccination Services.

Advanced services are those described within the NHS Community Pharmacy Contractual Framework and community pharmacies can choose to provide any of these services as long as they meet requirements set out in the Secretary of State Directions. The six advanced services included are: Medicines Use Reviews, Influenza Vaccinations, New Medicine Service, Appliance Use Review, Stoma Appliance Customisations and NHS Urgent Medicine Supply [90].

Although all of these services are available to PWD, they are not specifically tailored to, and staff are not trained to accommodate their particular needs meaning that the services currently on offer in community pharmacies (such as the medicines use reviews and new medicines service) are not being as effective as they could be to help PWD manage their medicines.

As with much health services research, the evidence base (both in regards to cost-effectiveness and clinical effectiveness) for these services is not robust, which was highlighted in a recent rapid evidence review of community pharmacy services [91]. Most

community pharmacy interventions also tend to be poorly designed (such as training requirements and time restrictions) and inadequately tested prior to implementation which does not follow the recommended approach for designing complex interventions [92].

Table 2 summarises some of the current evidence available for some of the routinely implemented services found in community pharmacies in the UK which clearly shows how there is a dearth of evidence for these services.

However, the rapid evidence review of community pharmacy services summarised findings that most services were shown to be effective and that LC services should be commissioned providing cost of service delivery is comparable with service provision from other providers [91].

Table 2. Current evidence of community pharmacy services

Service	Study Description	Key results	Critical Notes
		Essential Services	
Repeat dispensing	Systematic review, 2006 [93]	Four randomised controlled trials (RCT), 1 before-and-after study included. High patient satisfaction, more convenient and time saving.	Few studies included. Outcomes unable to be compared meaning definitive conclusions about effectiveness and impact of service difficult to make.
		Locally Commissioned Services	
Emergency Hormonal Contraception (EHC)	Randomised, single-blind controlled trial of 2117 women attending 4 California clinics providing family planning services. 2001-2003 [94]	Pharmacy access group pregnancy rates did not differ to clinics (adjusted OR*: 0.98, 95% CI**: 0.58 to 1.64, p=0.93) and there was no rise in sexually transmitted diseases (adjusted OR*: 1.08, 95% CI**: 0.71 to 1.63, p=0.73) compared to clinics.	Results not statistically significant due to not reaching required sample size of 620 in clinic group so should be interpreted with caution. Based in California, unsure if would gain similar results in the UK due to differences in clinic and pharmacy locations and procedures.
Chlamydia screening & treatment	Systematic review, 2013 [95]	12 studies included. Pharmacies were reported to be accessible and convenient and pharmacists were competent.	No cost related outcomes reported. Small number of studies included.
Smoking cessation	Systematic review identifying interventions to manage alcohol misuse, smoking and overweight. 2016 [96]	12 RCTs included regarding smoking cessation. Behavioural support and/or nicotine replacement therapy effective and cost-effective. Pooled OR* of intervention effects for smoking cessation was 1.85 (95% CI**: 1.25 to 2.75).	Information available did not allow for moderations for age, sex, ethnicity and socioeconomic status. No information on how service delivered and perspectives of the pharmacy staff implementing service.
		Advanced Services	
New Medicines Service (NMS)	Pragmatic patient-level parallel RCT in 46 community pharmacies (n=504). 2015 [97]	In the adjusted intention-to-treat analysis, OR* for increased adherence was 1.67 (95% CI**: 1.06 to 2.62, p=0.027) in favour of NMS arm. General trend to reduce NHS costs with a saving of £21 (95% CI**: £59 to £100, p=0.128) per patient.	Primary outcome measure relied on self-report in an unblinded study which could have led to bias in the results and an increased level of self-reported adherence in NMS arm (as they are aware of what the service is meant to achieve).
Medicines Use Review (MUR)	A review of current evidence (2012) [98]	Lack of robust research evidence consistently demonstrating any cost or clinical effectiveness compared with traditional care. Medication reviews can be more effectively deployed in the future by targeting, multi-professional involvement and paying greater attention to medicines which could be safely stopped.	
Influenza Vaccination	Systematic review. 2010 [99]	44 RCTs included. Nurses or pharmacists providing vaccinations and related education increased the likelihood of vaccine uptake (pooled OR: 3.29, 95% CI, 1.91 to 5.66, p<0.001).	Quality of evidence for many of the outcomes was 'low' or 'very low'. Key result reported here only based on 2 RCTs and a small sample size.
	Service evaluation of the effectiveness and cost of vaccinations administered in pharmacies. 2016 [100]	On average, a pharmacy administered vaccine dose costs the NHS up to £2.35 less than a GP administered dose.	Only based in London pharmacies so results may not be generalisable to other areas of the country (such as the use of inflated pharmacist salaries for cost calculations).

***Key**: *OR: Odds Ratio; **CI: Confidence Interval*

In addition to these commonly implemented services, community pharmacies have also previously shown their potential for use in the support of chronic diseases such as hypertension [101], asthma [102, 103] and diabetes [104], yet little research has been conducted for how community pharmacies could support the chronic condition of dementia, which could help support some of the outcomes listed above in the NDD and the NICE guidelines.

Furthermore, an independent government review of clinical pharmacy services performed in 2015 has recommended that community pharmacies should have greater involvement in the management of long term conditions [105] and PWD has the potential to fit into this category. Carrying out this recommendation however would have to be done with considerable care and with large contributions from other primary care HCPs. This is because in the UK, GPs are incentivised and rewarded via the Quality and Outcome Framework (QOF) to provide high quality care to their patients and to help standardise improvements in the delivery of primary care. The QOF includes a wide range of indicators within 3 domains [106]:

- **Clinical domains**- which includes the identification, recording and ongoing management of medical conditions (such as heart failure and diabetes mellitus)
- **Public Health domain** – such as blood pressure, obesity and smoking
- **Quality Improvement domain** – such as prescribing safety and end of life care)

Each indicator (such as: '*BP002. The percentage of patients aged 45 or over who have a record of blood pressure in the preceding 5 years'*) receives points when a certain threshold is met which then determines the financial reward the GP practice will receive. Several of the QOF indicators (such as '*SMOK004. The percentage of patients aged 15 or over who are recorded as current smokers who have a record of an offer of support and treatment within the preceding 24 months'*) are tasks which could be or are also already conducted in community pharmacy (i.e. a smoking cessation service or a blood pressure service). Therefore, if community pharmacy continue to become more clinically orientated and offer more services, GP practices will be unable to meet some of their QOF thresholds and receive as much financial reward and this is something which must be considered in the future design of a community pharmacy intervention.

However, community pharmacies tend to be more accessible to patients in the community compared to GP surgeries with an estimated 89% of the UK population living within a 20 minute walk [107]. Additionally, with the current trend for technology to be used where

possible such as dispensing robots, community pharmacists are being driven to use their expert medicines knowledge to provide more person centred, patient facing care [105].

1.9.1 Section summary

In summary, the development of a novel community pharmacy intervention targeted at PWD and their carers could therefore help meet many of the NDD outcomes stated in section 1.7 but in particular outcome 2:

'I know that services are designed around me and my needs'

Although services are beginning to emerge for a variety of chronic health conditions and the community pharmacy role is becoming more patient facing, there is still no intervention designed around PWD and their needs. In designing such an intervention, stakeholders should be involved to ensure that the intervention does not conflict with other HCP services and incentives.

1.10 Designing a complex intervention

Complex interventions are widely used in the health service and are defined as interactions with several interacting components [92].

Many existing interventions in community pharmacy could be classed as a complex intervention, as would a newly developed intervention targeted at PWD and their carers.

Complex interventions can be difficult to evaluate and so The Medical Research Council (MRC) provides guidance for how complex interventions should be developed with the use of 4 keys steps (see Figure 4).

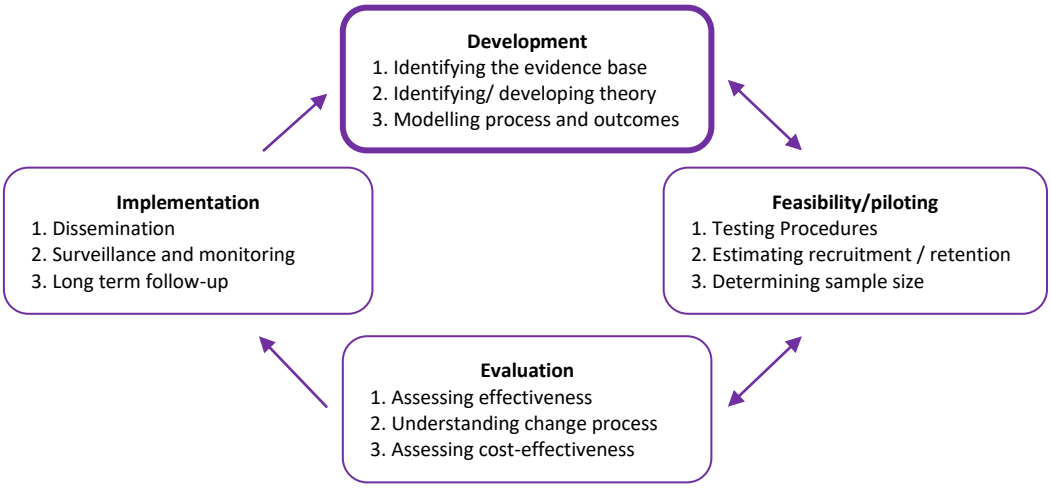

Figure 4. Medical Research Council process summary for developing a complex intervention

Following this guidance, the first step to this process for developing a successful community pharmacy intervention targeted at PWD is the **development of the intervention**. The development stage involves:

- **Identifying the evidence base:** Ideally carry out a systematic review to identify the relevant existing evidence base.
- **Identifying / developing appropriate theory:** Develop a theoretical understanding of the likely process of change by interviewing stakeholders and drawing on existing evidence and theory.
- **Modelling process and outcomes:** This can provide information about the design of the intervention and may identify weaknesses that need refinement.

For an intervention to be developed, it is therefore important for these stages to be addressed prior to moving to the feasibility/ piloting step and this is where this thesis will be concentrated.

1.11 Logic Model for community pharmacy tool

Logic models have been proven to be a successful tool for the planning, implementation and performance management in primary care [108-110]. They are defined as a graphical representation of how a program/intervention is intended to work and links outcomes with processes and any theoretical assumptions [111]. They show what the program/ intervention will do and what it will accomplish by way of desired outcomes [112].

Rohwer et al. explains that logic models can be used to help authors to explicitly address and make sense of complexity, adding value by achieving a better understanding of the interactions between the intervention, its implementation and its multiple outcomes among a given population and context. They can therefore improve communication between producers and potential users of research evidence [113].

These properties can be useful during the design of complex interventions in health services research where there may be a variety of different researchers/ practitioners/ other stakeholders involved. Logic models provide a summary of the intervention, the context and rationale for the intervention, the possible outcomes and outcome measures in a way which is accessible to all and does not require a large amount of time to read.

Another advantage of logic models is that they have the ability to adapt and evolve. This means that as knowledge in a given area increases, the model can change which allows the model to remain current and of continued benefit to both researchers and stakeholders.

Conversely, it has been argued that logic models can become a rigid statement of the developing plan and thereby limit the program's (but in this context, intervention's) responsiveness to new information [114].

Logic models are increasingly being used within health services research [115, 116] and a logic model shall be developed throughout this thesis as a way of illustrating and summarising how the findings from each chapter contribute to the development of a future community pharmacy intervention targeted at PWD. The logic model will provide a graphic representation of how the findings from each study build on each other to create the potential intervention and what potential process measures, clinical and humanistic outcomes may occur as a result.

1.12 Chapter Summary

As the number of people living with dementia increases, so are the numbers of PWD living in their homes accessing primary care services. Community pharmacies are within easy reach of most people within the community and with the community pharmacy role becoming more clinical and patient focussed, there is the potential for community pharmacies to deliver an intervention targeted at PWD and their carers.

Pneumonia is one of the leading causes of hospitalisation and death amongst PWD and has many risk factors such as the presence of dysphagia and the types of medicines prescribed. A community pharmacy intervention may be able provide further medicines support to PWD by exploring some of the potential risk factors for PWD developing pneumonia by such methods as checking the appropriateness of the medicine formulation and supporting the safe swallowing of medicines.

The first version of the logic model for this study is illustrated in Figure 5 which contains the basic information based on this introductory chapter.

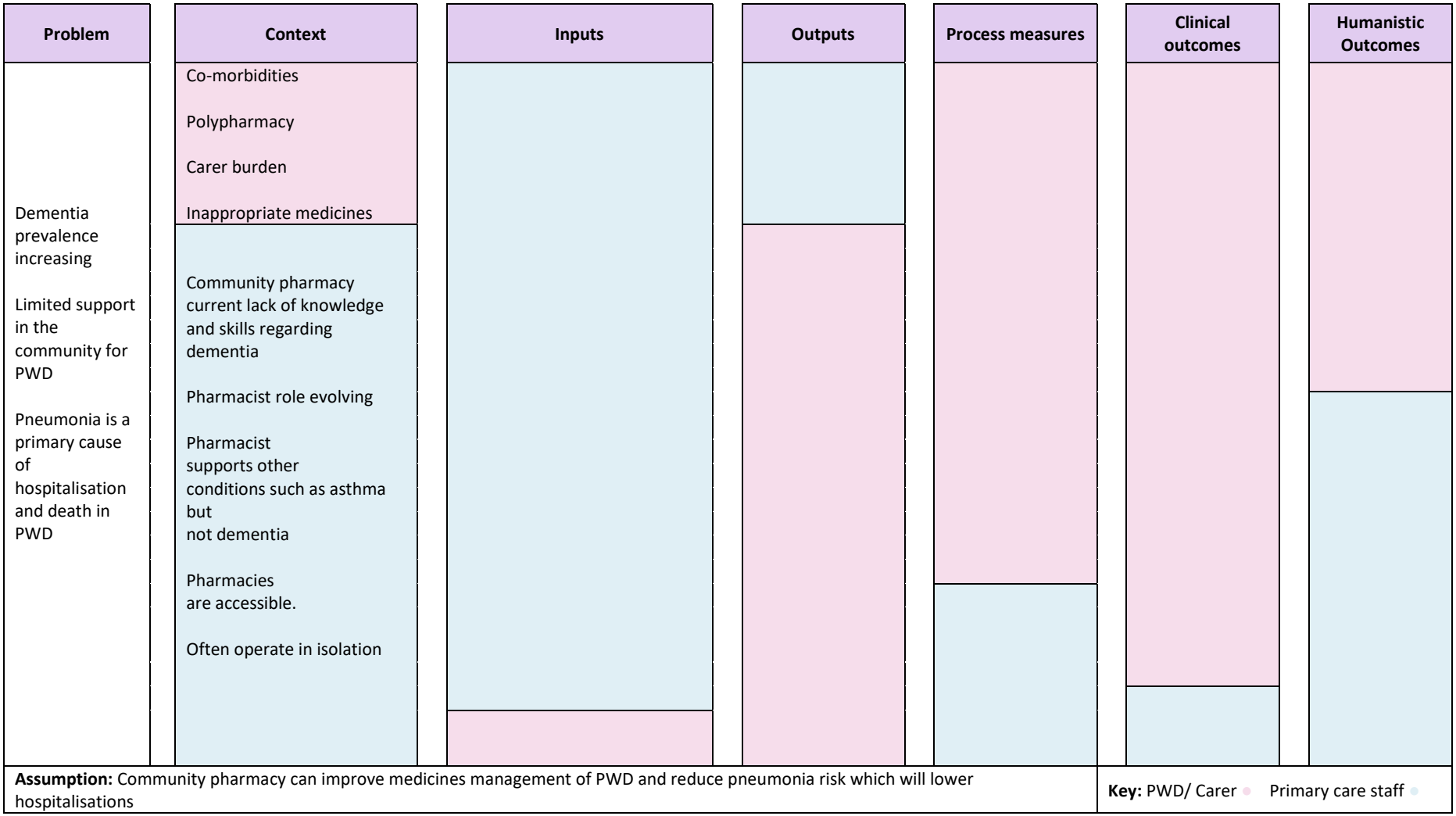

Figure 5. Initial logic model.

1.13 Study Aims and Objectives

With a growing number of community dwelling PWD who are being prescribed a number of medicines, and the increasing number of interventions being delivered by community pharmacists for a range of healthcare conditions, there is scope for community pharmacies to offer an appropriately designed intervention targeted to PWD. This thesis therefore explores what a community pharmacy-based intervention for PWD should ideally consist of. Within this we need to consider how they can best help with medicines management to support people to remain in their own home for longer and ensure that medicines do not contribute to the pneumonia related morbidity and mortality.

Aim

The aim of this study and PhD is to develop the evidence base and theory to underpin the development of a community pharmacy intervention which supports and enhances the medicines management of people affected by dementia and who live at home in the community.

Objectives

1. To identify the types of interventions that have already been trialled in PWD which use members of the pharmacy team and their effective and ineffective elements.
2. To identify any potentially modifiable risk factors for pneumonia within a community pharmacy setting.
3. To explore how people with mild-moderate dementia are currently managing their medicines at home within the community without the help of a paid carer.
4. Complete a logic model for a proposed community pharmacy intervention.

Objective 1 shall be met by conducting a narrative review which will also critique the identified studies and provide an insight into the current quality of studies undergone in this field. Objective 2 shall be met by using a case-control study design which will enable the associations of a variety of potential risk factors to be determined with a singular outcome (pneumonia). Objective 3 shall be met by using observations which will allow for the exploration of how PWD currently manage their medicines within the context of their own homes

Chapter 2.

Systematic review with narrative synthesis

2.1 Chapter Overview

This chapter aims to meet objective 1 of the study's aims and objectives which are set out in section 1.13: 'To identify the types of interventions that have already been trialled in PWD which use members of the pharmacy team and their effective and ineffective elements.'

This chapter identifies the various types of interventions by undergoing a systematic review with a narrative synthesis. The interventions and their results were categorised, described and searched for reported effective and ineffective elements in the hope that the knowledge gained will help to develop an appropriate intervention for PWD. In addition to this, the studies were assessed for quality to provide the reader with an overview of how meaningful the reported results were.

2.2 Background

There were a number of review-based approaches which could have been used to identify the types of interventions that have already been trialled in PWD such as a critical review, narrative review and a systematic review.

Critical reviews go beyond describing the identified studies by including a degree of analysis and conceptual innovation. The review can then be used as a 'launch pad' for a new phase of conceptual work development and subsequent testing. However, there is no formal requirement for them to conduct a systematic search or to present their methods of search, synthesis or analysis explicitly and there is no formal quality assessment [117]. This means that not all potential and relevant studies would likely be identified or included and that the results are open to bias as studies could potentially be omitted (either knowingly or inadvertently), which makes this approach inappropriate for this study.

Another type of review which could be used to identify the relevant studies to aid the development of a future community pharmacy intervention is a narrative review. Narrative reviews use broad research questions and do not have to use an explicit search approach or criterion-based selection method. Critical evaluation of the studies does not have to be rigorous and is variable dependent on the review [118]. Using a narrative review approach would suit the anticipated broad research question and qualitative extracted data but similarly to a critical review, this approach does not require a systematic approach to identifying and analysing relevant studies and lacks an explicit intent to maximise scope.

This means that this approach is also open to potential bias from studies potentially not being included [117].

A systematic review (SR) attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimise bias and often contains meta-analyses of study results [119-121]. SRs have:

- Clearly stated objectives with pre-defined criteria for studies
- Explicit, reproducible methodology
- Systematic search to identify all studies that would meet the eligibility criteria
- Assessments of the validity of findings of the included studies
- A systematic presentation and synthesis of the characteristics and findings of the included studies.

The MRC guidance outlined in section 1.13 detailed how during the development stage of a complex intervention, a systematic review (SR) should ideally be carried out to identify the relevant existing evidence base [92]. The tools used to conduct a systematic review ensure that all potential relevant studies are included and ensures that there is no bias in the final studies selected for inclusion which makes the study more credible.

To meet objective 1 and to follow MRC guidance, it was therefore desirable and most appropriate to conduct an SR to systematically identify all current and previous interventions targeted to PWD.

The qualitative nature of the data to be extracted meant that a meta-analysis of the data would not be possible and instead, narrative synthesis would be conducted, which has been the reported approach in a number of other systematic reviews [122-124].

This study will therefore use a systematic approach for the identification and evaluation of studies and narrative synthesis for the analysis of studies to identify and evaluate the existing evidence for pharmacist interventions from within community pharmacy targeted to PWD in order to develop a thorough theoretical understanding of any future intervention.

This SR will enable an understanding of interventions that utilise members of the pharmacy team which have already been trialled to be gained and what aspects of the intervention were effective, and which could be improved.

2.3 Aims and Objectives

Aim

The initial aim of this qualitative SR was to identify and evaluate the current research of interventions aimed towards patients affected by dementia that utilise a member of the community pharmacy team.

Objectives

The initial objectives for this SR were to:

- Describe the extent and nature of the interventions within community pharmacy which use a member of the community pharmacy team
- Identify the effective and ineffective elements from the studies
- Identify the key outcome measures
- Describe the key results
- Assess the quality of the research conducted

2.4 Methods

2.1.1 Scoping review

A scoping review was initially performed using a similar methodology and search strategy to this SR (Appendix 1 and 2) which was designed to:

- Review initial results and findings
- Refine inclusion and exclusion criteria
- Test data extraction process
- Refine data collection process
- Refine objectives for the SR

The protocol for the scoping review was submitted and can be seen at PROSPERO (2015: CRD42015026028).

The scoping review found just three studies which met the inclusion criteria. Of these, two were memory screening services and one was an audit of the various interventions community pharmacy staff had had with PWD. Following the low number of studies included in the scoping review, the following changes were made to the method of the SR:

- Inclusion criteria were broadened to include studies where the majority of service recipients had dementia.
- The intervention was broadened to include any pharmacy team member from any work sector (such as hospital, outpatient clinic, community pharmacy).
- Outcome measures would be categorised using the ECHO (Economic, Clinical and Humanistic Outcomes) model [125].
- The setting was broadened to include any setting where a pharmacy team member was present.
- Search terms were amended to reflect the above changes to the inclusion criteria (scoping review search terms in appendix 2).
- NHS evidence was additionally searched for studies.
- The extraction tool was amended to ensure all relevant data was recorded.
- Effective and ineffective elements from scoping review studies were reviewed and developed into the extraction tool.
- The GRADE Working Group (Grades of Recommendation, Assessment, Development and Evaluation Working Group) approach as suggested by Cochrane [126] was introduced and the quality assessment checklist amended for a more objective method to allocate a grade of quality to each study. GRADE covers a range of quality measures (including risk of bias) and was used to provide some more structured, objective method of reporting bias and quality which is advised by Cochrane. Further information on GRADE can be found in section 2.3.8.

The revisions above also led to minor changes to the aims and objectives for the SR. The protocol for the SR was also submitted to PROSPERO on 13.07.2016 (PROSPERO 2016: CRD42016042787).

Revised Aim

To identify and evaluate the current research of interventions aimed towards patients affected by dementia that utilise a member of the pharmacy team.

Revised Objectives

- Describe the extent and nature of the interventions
- Identify the humanistic, process, clinical and economic outcome measures used to determine effectiveness and cost-effectiveness
- Identify the key humanistic, process, clinical and economic results used to describe the effectiveness and cost-effectiveness of the interventions

- Identify the effective and ineffective elements
- Assess and grade the quality of the research conducted

2.4.1 Inclusion criteria

The inclusion criteria was set by using the PICOS (Population, Intervention, Comparator, Outcome, Setting) method as suggested in the Cochrane guidance [127].

Population

Studies were included where there was a minimum of 70% prevalence of dementia within the targeted population. This was to help broaden out the criteria to allow for a larger number of potentially informative interventions to be identified whilst maintaining that the interventions were targeted towards those affected by dementia. I.e. This approach allowed for a larger number of potentially relevant interventions to be included whilst ensuring that the predominant population of interest were those with dementia.

Intervention

The intervention was required to be conducted by a member of a pharmacy team including pharmacists, dispensers, accuracy checking technicians and pharmacy assistants. Where the intervention was conducted by a multidisciplinary team, the pharmacy team member was required to have a role which involved processes designed to improve patient outcomes such as patient counselling, identifying potential medicine interactions, conducting the training to other staff.

Comparator

No comparators were applicable for this type of review.

Outcome

Due to not wanting to limit the findings in this review and wanting to include all possible interventions which could have use in community pharmacy, outcome measures were not specified for paper inclusion.

Setting

Interventions were included from any setting where a pharmacy team member was present.

Types of studies

All study designs were included, and any form of published data would be accepted. This included conference abstracts, service evaluation reports and research journal articles.

Studies were included from any country and in any language (as long as the data could be translated) and from any date up to the date that data screening occurred. The broad inclusion criteria was to ensure that every potential intervention was captured.

2.4.2 Exclusion criteria

Studies were excluded if the same piece of research was reported in more than one article, as they would essentially be duplicates. Conference abstracts were also excluded if an updated report of results (for instance, a full article) was found which contained more information. Articles were also excluded where no results were reported (such as a protocol article).

2.4.3 Literature search strategy

Search terms

The PICOS method [127] was used in order to develop appropriate search terms (Appendix 3). Boolean operators and truncations were used where necessary.

2.4.4 Search methods for identification of studies

Database searches

The following databases were used to search literature with no language or date restrictions:

- Ovid MEDLINE® In-Process & Other Non-Indexed Citations and Ovid MEDLINE® 1946 to present*, OvidSP
- EMBASE, 1974 to present, OvidSP*
- CINAHL Complete, EBSCOhost

*The searches in MEDLINE and EMBASE were run simultaneously due to the OvidSP search engine having access to both databases.

Searching other resources

Grey literature searches were also conducted by using the same search terms as for the previous database searches (Appendix 3) at www.opengrey.eu.

The bibliographies of the included studies chosen for data extraction were additionally reviewed in order to identify any further potential references.

NHS evidence was searched which was accessed at https://www.evidence.nhs.uk. The same search terms were used as for the opengrey search but results were restricted to: 'Primary research', 'Drug/medicine management' and 'Policy and service development' for types of information and 'Public health', 'social care', 'clinical' and 'drugs and technologies' for area of interest.

2.4.5 Selection of studies

Results from each search were exported into the reference manager Endnote X7.2.1 and duplicates were removed. There were three key stages to the selection of studies:

1. **Initial screening of titles for relevance to research question.** This was carried out simultaneously by two independent researchers R1 and R3. R3 was not involved in any other part of this study and had limited knowledge of this study area.

2. **Abstracts screened against the inclusion criteria for selected titles.** This was conducted independently by two researchers R1 and R2 simultaneously. The criteria to identify papers for full text retrieval consisted of:
    - Empirical data available
    - >70% targeted to dementia affected participants
    - Pharmacy team member conducts intervention
    - Intervention present

    Reasons for inclusion and exclusion were documented on a specifically designed form created and managed in Microsoft Excel (see excel spreadsheets supplied electronically with this thesis).

3. **Assessment of full papers for inclusion in the review**. Reasons for inclusion and exclusion at this stage used the same criteria as stage 2 and were also documented in the same method. Like with stage 2, this was conducted independently by R1 and R2 simultaneously.

Any discrepancies between R1 and R2/R3 were resolved by discussion. A Cohens Kappa coefficient was calculated at each stage in order to assess inter-rater agreement.

2.4.6 Data Extraction

Extracted data was recorded in Microsoft Excel using an extraction tool specially designed for the reviews which was based on guidance from the Cochrane Effective Practice and Organisation of Care (EPOC) Review Group Data Collection Checklist [128].

The extraction tool collected the following data during the SR where possible:

- **Study details**: Author; year; study design; country; study setting; inclusion and exclusion criteria; sample size; recruitment methods and use of written consent
- **Nature and extent of intervention**: Type of intervention; intervention description and details; involvement of other HCPs; target population; follow up.
- **Outcome data measures**: Identified and reported outcome measures categorised based on ECHO [125]. Due to the anticipated nature of the outcome measures, a fourth category, 'Process' was added in order to capture outcome measures which are not seen within ECHO (Table 3).

Table 3. ECHO definitions

ECHO category	Definition	Additional potential outcomes
Economic	Total costs of medical care * associated with treatment alternatives * balanced against clinical or humanistic outcomes.	Any other costs reported which may include medical, non-medical and indirect (productivity) costs
Clinical	Medical events that occur as a result of disease or treatment *	Clinical indicators such as measurements of a patient's physical and biomedical status
Humanistic	Functional status or quality of life	Effects of disease or treatment* on humanistic outcomes

**Or intervention in the case of this SR*

- **Effective and ineffective elements:** Elements described by the authors as effective or ineffective regarding their intervention and study design were identified and categorised where possible.

R1 was responsible for the input of all data into the extraction tool. A small sample (approximately 15%) of this data was reviewed for accuracy by R2.

The full details of what information was collected during the SR can be seen in Appendix 4.1.

2.4.7 Data Analysis

Due to the wide scope and qualitative nature of this review, statistical methods and meta-analysis were not appropriate and therefore narrative synthesis was used which consisting of discussions of the studies' characteristics and findings [129].

2.4.8 Assessment of quality

The methodologies were critiqued for bias and quality by the use of an assessment checklist tool which was created by using guidance from the 2009 PRISMA (Preferred Reporting Items for SRs and Meta-Analysis) checklist tool [130]. Cochrane advises that in systematic reviews, the quality of the studies should be assessed using the GRADE approach so this was also incorporated into the checklist tool [126].

GRADE

The results and overall quality of each study selected for data extraction were graded based on the GRADE.

GRADE initially rates studies as HIGH, MODERATE, LOW or VERY LOW based on their study design. Table 4 summarises the 5 factors that can cause a study to be downgraded [131]. Studies can also be upgraded in the following instances:

- Large magnitude of Effect
- Dose Response
- Effect of all plausible confounding factors would be to reduce the effect (where an effect is observed) or suggest a spurious effect (when no effect is observed).

Table 4. GRADE downgrading factors

Downgrade factor	Examples
Reporting Bias	Unreported results for stated outcome measures.
Inconsistency	Inconsistency of results or unexplained heterogeneity.
Indirectness	Indirect population (population restricted or inclusion of people outside of interest, small number of comparators, short follow-up), unclear outcomes or irrelevant outcomes.
Imprecision	Small sample size, small effect size, total number of events <300, wide confidence intervals.
Limitations in design	High number of limitations, high likelihood of bias in study design.

Due to the majority of studies anticipated to be small service evaluations and the upgrade criteria not to be relevant in most cases, it was decided that the upgrading of studies would

occur if the converse to the downgrading factors was present (no publication bias, very consistent, very precise, very direct and minimal limitations).

It should be noted that GRADE rates the quality of evidence of each outcome separately. For the purpose of this review where there are no set outcome measures, is must be iterated that GRADE was used for guidance only. Therefore, although the suggested grading factors were utilised, each study was graded as a whole rather than for each outcome measure.

Input software

All data assessing and grading the quality of the studies was recorded in the assessment template tool developed and managed in Microsoft Excel. Full details of what was recorded can be seen in Appendix 4.2. As with the extraction tool, R1 inputted all data with R2 periodically reviewing the spreadsheet for accuracy and relevance.

2.5 Results

2.5.1 Scoping Review Results

Figure 6 summarises the results from each stage of the data selection process and Table 5 shows the level of agreement between the two independent raters, as described by Landis and Koch [132], at each stage.

Of the three studies selected for data extraction, two are presented as research articles (Breslow [133], Rickles et al. [134]) and one is presented as a conference abstract (Manrai et al. [135]).

Breslow [133] and Rickles et al. [134] were both testing the feasibility of a memory screening service within community pharmacy whilst Manrai et al. [135] summarised the various roles that pharmacy team members (mainly technicians) have within a community pharmacy to patients with dementia.

The complete extraction and quality assessment results for these three studies are reported later on in this chapter as they were also included in the SR.

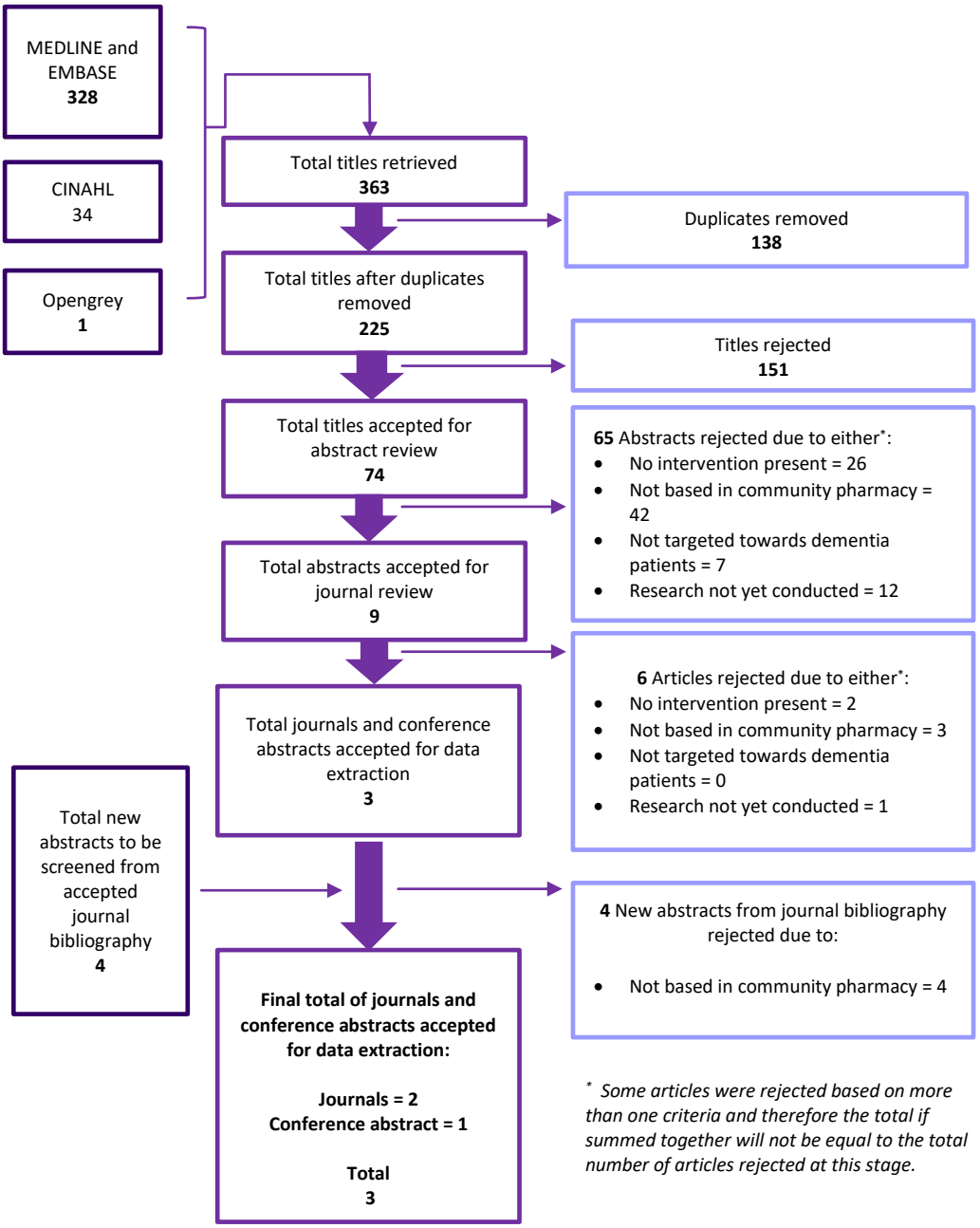

Figure 6. Data selection flowchart for scoping review

Table 5. Cohen's Kappa scores for each data selection phase for scoping review

Stage	Cohen's Kappa (κ)	Level of agreement
Title	0.65	Substantial
Abstract	0.58	Moderate
Article	0.53	Moderate

2.5.2 Systematic review with narrative synthesis Results

2.5.2.1 *Literature search*

There was a total of 1250 citations returned from the initial literature search of which 29 studies met the inclusion criteria. The results from each stage of the screening process are reported in Figure 7. The most common reason for exclusion at the abstract screening stage was no intervention present whereas at the full text screening stage, the most common reason was a non-dementia specific target population.

Ten new potential references were found during the selected articles bibliography search. However, after further screening, all ten references were unsuitable for data extraction with the most common reason being that there was no pharmacy team member present.

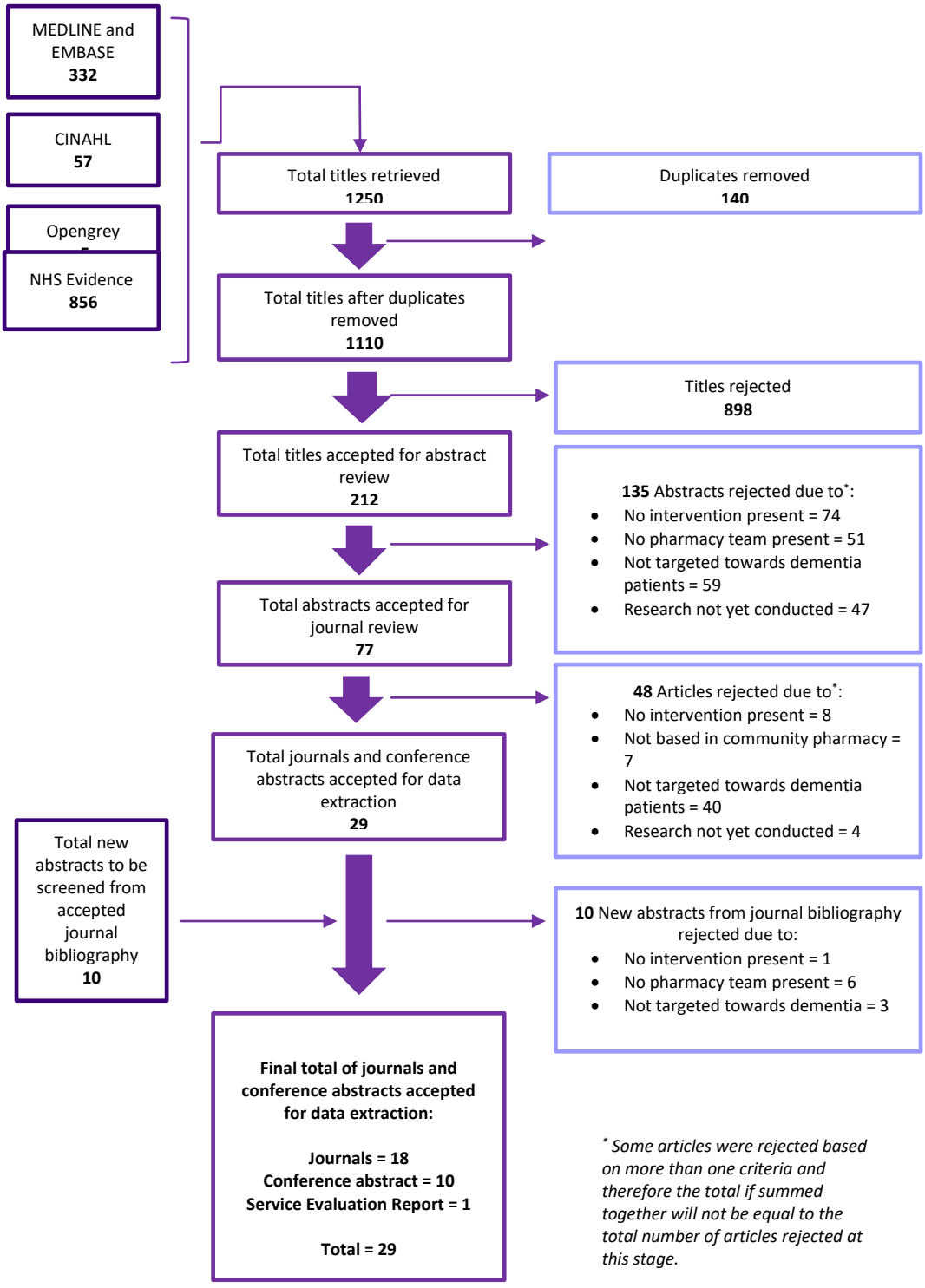

Figure 7. Flow diagram for data selection for systematic review

2.5.2.2 *Cohens Kappa results*

Table 6 shows the associated Cohens Kappa results for each stage of the screening process between R1 and R2.

Table 6. Measure of agreement between each rater for narrative review

Stage	Cohens Kappa result	Level of agreement
Title Screening	0.36	Fair
Abstract Screening	0.43	Moderate
Journal Screening	0.52	Moderate

2.5.2.3 *Study characteristics*

Tables 7 and 8 summarise the key study characteristics for the 29 studies which includes 7 conference abstracts [135-141], service evaluation independent report [142] and one article which was written in French [143].

A variety of settings were found in the studies including community pharmacy [133-135, 142, 144], care/nursing homes [136-138, 145-148] and clinics [139, 149-152]. The total number of settings ranged from 1 [135-139, 143, 144, 146, 147, 150-158] to 100 [159] with two studies having an unknown number [140, 160].

2.5.2.4 *Inclusion Criteria*

The broad nature of this SR has led to a wide variation in inclusion criteria. The common themes are summarised in table 5 with some of the 'other' criteria for inclusion being: at risk of developing delirium [157]; receive a monitored dosage system and/ or have a dementia diagnosis [135]; have completed a PHASE-20 questionnaire [161]; have adequate vision and dexterity to load a pillbox [151] and have had ≥2 inpatient admissions in the last year or ≥3 emergency department visits in the last year [154].

Table 7. Summary of study characteristics

Author	Year	Study Design				Conference Abstract	Country
		Service Evaluation	Case Study	Cross Sectional	Other		
Cations [141]	2015	✓				✓	Australia
Kröger [148]	2014	✓					Canada
Monette [146]	2004	✓					Canada
Mouchoux [143]	2011	✓					France
Collier [136]	2013	✓				✓	Ireland
Conlon [137]	2009-10	✓				✓	Ireland
Nakamura [149]	2012-14	✓					Japan
Watanabe [155]	2008-12	✓					Japan
Efjestad [153]	2011	✓					Norway
Stuhec [140]	2013	✓				✓	Slovenia
Gustafsson [161]	2012	✓					Sweden
Anonymous [142]	2014-15	✓					UK
Child [162]	2011	✓					UK
Maidment [138]	2011	✓				✓	UK
Breslow [133]	2013	✓					USA
D'Souza [158]	2010-12	✓					USA
Frausto [154]	2013-14	✓					USA
Hursh [147]	2008-09	✓					USA
Paquin [157]	2010-12	✓					USA
Patel [139]	2010	✓				✓	USA
Rickles [134]	2008	✓					USA
Farrell [156]	2013		✓				Canada
Sakakibara [150]	2014				✓*		Japan
Furniss [145]	2000				✓**		UK
Manrai [135]	2015				✓#	✓	UK
Anderson [151]	2014			✓			USA
Fountain [144]	2007		✓				USA
Setter [159]	2004-05			✓			USA
Sonnett [152]	2012			✓			USA

**Non-randomised intervention study; **Randomised-controlled trial; #Audit*

Table 8. Summary of Study characteristics - continued

Author	Setting	Total Settings	Inclusion Criteria set for each study						
			Dementia diagnosis	Prescribed certain medication	Referred to/attending certain setting or receiving particular service	Resident in care/nursing home	Potential dementia diagnosis	Certain Age	Other
Collier [136]	Care/nursing home	1				✓			
Conlon [137]	Care/nursing home	1				✓			
Furniss [145]	Care/nursing home	14				✓			
Hursh [147]	Care/nursing home	1				✓			
Kröger [148]	Care/nursing home	3	✓			✓			
Maidment [138]	Care/nursing home	1	✓			✓			
Monette [146]	Care/nursing home	1	✓	✓		✓			
Anderson [151]	Clinic	1							✓
Nakamura [149]	Clinic	5	✓	✓					
Patel [139]	Clinic	1			✓				
Sakakibara [150]	Clinic	1			✓			✓	✓
Sonnet [152]	Clinic	1			✓				✓
Setter [159]	Community dwelling	100			✓		✓	✓	
Anonymous [142]	Community Pharmacy	20	✓				✓		
Breslow [133]	Community Pharmacy	2					✓	✓	
Fountain [144]	Community Pharmacy	1	Not applicable due to being a retrospective case study of one patient						
Manrai [135]	Community Pharmacy	1	✓						✓
Rickles [134]	Community Pharmacy	12					✓		
Gustafsson [161]	Geriatric care unit	?							✓
Child [162]	GP Surgery	60	✓	✓					
Stuhec [140]	GP Surgery	?	✓		✓				
Efjestad [153]	Hospital (all)	1		✓	✓				
Farrell [156]	Hospital Inpatient	1			✓				
Frausto [154]	Hospital Inpatient	1	✓	✓				✓	✓
Mouchoux [143]	Hospital Inpatient	1			✓				
Paquin [157]	Hospital Outpatient	1	✓	✓				✓	✓
Watanabe [155]	Hospital Outpatient	1	✓		✓				
D'Souza [158]	Medical centre	1	✓					✓	✓
Cations [141]	Residential aged care facility	24		✓				✓	✓

2.5.2.5 *Recruitment*

Table 9 summarises the recruitment methods used and which eight studies received written consent. Participants tended to be recruited automatically into studies due to their study design. Sample size varied between a range of 1 and 895 with two studies [135, 142] having an unknown size.

Table 9. Summary of recruitment methods, arranged by sample size

Author	Sample size	Recruitment method					Written Consent
		HCP request	Advertising (e.g. posters, brochures)	Referral	Screening	Automatically recruited if meet criteria	
Anonymous [142]	?	✓*		✓			X
Manrai [135]	?					✓	X
Farrell [156]	1					✓	X
Fountain [144]	1			✓			X
Patel [139]	20					✓	X
Breslow [133]	26		✓				✓
Maidment [138]	26					✓	X
Nakamura [149]	35				✓		X
Kröger [148]	48	No information available					X
Efjestad [153]	50					✓	X
Sakakibara [150]	50					✓	✓
Collier [136]	54					✓	X
Conlon [137]	67					✓	X
Child [162]	70				✓		X
Cations [141]	81					✓	X
Monette [146]	90				✓		✓
Mouchoux [143]	97					✓	X
Setter [159]	100				✓	✓	✓
Watanabe [155]	111	✓**				✓#	X
Frausto [154]	128					✓	X
Hursh [147]	~130					✓	X
Anderson [151]	150		✓				✓
Rickles [134]	161	✓	✓	✓##			✓
D'Souza [158]	162			✓			X
Sonnet [152]	302	✓					✓
Furniss [145]	330	Homes randomised for control and intervention. All patients that consented in intervention arm were recruited					✓
Paquin [157]	501				✓		X
Stuhec [140]	629					✓	X
Gustafsson [161]	895	✓					X

**Or invited to consultation without referral if signs are noticed by primary care navigator; **Intervention patients: recommended to attend Donepezil Outpatient Consultation Service (DOCS) by physician; #Controls: patients prior to DOCS established; ##Self-referral*

2.5.2.6 *Interventions*

The results from this SR shows that a range of interventions have been researched for patients that are affected by dementia. The interventions were categorised by R1 and reviewed by R2 into: medication review; targeted medicine intervention; education; memory screening and miscellaneous.

Medication Reviews

Thirteen studies (45%) were for varying forms of medication reviews (see Table 10) and was the most common type of intervention identified. The studies by Collier et al. [136] and Conlon et al. [137] involved the pharmacist in weekly, interdisciplinary medication reviews whilst the service evaluated by D'Souza et al. [158] incorporated a variety of interventions which included medication reviews by pharmacists and nurses and weekly interdisciplinary meetings.

Farrell et al. [156] conducted medication reviews independently with little input on their decisions from a healthcare team whereas Fountain et al. [144] conversely had input from an interdisciplinary team following the conducting of a medication review during home visits.

Frausto et al. [154] described how their clinical pharmacy specialist had a face-face meeting with the inpatient prior to discharge and then a further telephone call. Recommendations were then made to either the inpatient team or primary care provider.

Furniss et al. [145] investigated the effect of a medication review of nursing home residents by a pharmacist.

Gustafsson et al. [160] examined the use of a medication review for reducing the number of various inappropriate drugs such as non-steroidal anti-inflammatories, anticholinergics and antipsychotics. Kröger et al. [148] and Mouchoux et al. [143] conducted medication reviews when patients were admitted to their units followed by interdisciplinary team meetings. Paquin et al [157] conducted not only a medication review, but additionally a medication safety check via a checklist and a follow-up telephone call post discharge.

Stuhec et al. [140] also targeted specific medicines during a clinical pharmacist led review but in this case it was the appropriate doses of AD medicines.

Patel et al. [139] on the other hand, described the outcomes of having a clinical pharmacist comprehensively review patients charts at a Memory Clinic.

Table 10. Medication Review category intervention details

Author	Pharmacist Medication Review Intervention Details									Target Population*		Follow-up
	Other multidisciplinary team members involved**				Involves talk with patient/ family members/nursing home staff	Use of designed checklist/guidance tool to aid review	Review targeting specific medicines	Telephone call	Home visit	>70%	100%	
	D	N	S	O								
Collier [136]	✓	✓					✓			✓		✓
Conlon [137]	✓	✓					✓			✓		✓
D'Souza [158]	✓	✓	✓		✓			✓	✓	✓		✓
Farrell [156]					✓						✓	
Fountain [144]	✓	✓#	✓						✓		✓	
Frausto [154]	✓	✓			✓			✓##			✓	
Furniss [145]					✓					✓		✓
Gustafsson [160]	✓	✓					✓			✓		
Kröger [148]	✓	✓			✓	✓	✓			✓		
Mouchoux [143]	✓	✓	✓	✓^			✓				✓	
Paquin [157]					✓	✓		✓		✓		✓
Patel [139]										✓		
Stuhec [140]	✓						✓				✓	

**Target population consisted of patients with dementia in >70% of sample size or 100% of sample size; **D=Doctor/General Practitioner/Physician/geriatrician, N=Nurse, S=social worker/caseworker; #Nurse's aide; ##Reconciliation to primary care prover conducted by phone*
^Including physiotherapists, occupational therapists, music therapists and speech therapists

Targeted medicine intervention

Seven studies targeted or concentrated on specific medicines and utilised a range of intervention methods rather than simply completing a more comprehensive medication review.

Cations et al. [141] targeted their intervention on the deprescribing of antipsychotics in behavioural and psychological symptoms in dementia (BPSD). These are symptoms common in PWD and explained in greater detail in Chapter 1, section 1.5.2. Child et al. [162] similarly identified and reviewed all patients on a local dementia register prescribed antipsychotics with the aim to deprescribe where possible.

Efjestad et al. [153] targeted medicines with anticholinergic properties and created an anticholinergic drug scale (ADS) score for each patient in order to determine what changes could be made.

Hursh et al. [147] utilised an interdisciplinary team to identify and then change the high prevalence of antipsychotic use by implementing a range of interventions such as staff education, use of non-pharmacological measures and improving the use of documentation tools.

Maidment et al. [138] also targeted the inappropriate use of antipsychotics using the US OBRA guidelines and a specialist pharmacist reviewed these medicines and alternative solutions were developed where possible.

Nakamura et al. [149] utilised a pharmacist in a different way. Their pharmacist used a checklist, questionnaire and rapid saliva swallowing test to assess patients on a low dose of Donepezil and their carers to determine whether the PWD should have their dose increased.

Sakakibara et al. [150] was one of the few studies which was not a service evaluation and instead was a non-randomised intervention study which targeted the use of benzodiazepines. A pharmacist was responsible for reviewing and proposing changes to these medicines in the intervention group.

Key therapeutic areas

Within both the medication review and targeted medicine intervention categories, the use of antipsychotics, anticholinergics or benzodiazepines in PWD emerged as key themes. Table 11 summarises studies these findings.

Author	Antipsychotics	Anticholinergics	Benzodiazepine
		Medication Reviews	
Collier [136]	✓		
Conlon [137]	✓		
Fountain [144]		✓	
Furniss [145]	✓		✓
Gustafsson [160]	✓	✓	✓
Mouchoux [143]	✓	✓	✓
Paquin [157]	✓	✓	✓
Patel [139]		✓	
		Targeted medicine intervention	
Cations [141]	✓		
Child [162]	✓		
Efjestad [153]		✓	
Hursh [147]	✓		
Maidment [138]	✓		✓
Sakakibara [150]			✓

Table 11. Studies where antipsychotics, anticholinergics or benzodiazepines were a key theme

Education

Three research studies explored the impact of further education. Monette et al. [146] and the Primary Care Navigators (PCN) report [142] both provided further training for various health professionals ranging from nurses, psychiatrists, pharmacists and pharmacy dispensers. Monette et al. [146] aimed to optimise the management of disruptive behaviours in nursing homes without necessarily resorting to antipsychotics. This was achieved by using an interdisciplinary educational programme involving: consciously highlight the problem, a series of educational sessions targeted to different HCPs and ongoing clinical follow-up.

The PCN report aimed to bridge the gap between PWD and their carers with local and national support services. The PCN report covered two levels of education. Firstly, the education of the GP and pharmacy staff by using e-learning, interactive study days and ongoing mentoring. Secondly, the provision of advice and education by the newly trained PCN to patients affected by dementia in the community by way of appropriate signposting.

Watanabe et al. [155] conversely, studied the impact of an increase in the provision of advice to patients newly prescribed donepezil. Adherence and an appropriate dosing

regimen are discussed in addition to further information about the medicine (such as what the medicine may do and how long it may take to work).

Although Patel et al. [139] was discussed briefly in the previous section relating to medicine changes, due to overlap the research also has a place in education as the study highlighted how the provision of advice to patients is part of a clinical pharmacist's daily activity.

Memory Screening

Four studies were targeted at patients at high risk of having dementia and explored the acceptability and appropriateness of a memory screening service within community pharmacies. Rickles et al. [134], Breslow [133] and Setter et al. [159] used only pharmacists to conduct their interventions whereas Sonnet et al. [152] reported how pharmacists conducted memory screening services at homebound patient's homes as part of a larger interdisciplinary intervention. Table 12 summarises the assessments that were completed for each intervention and whether there was any follow-up of participants.

Table 12. Summary of memory screening interventions

Author	Memory screening intervention by a pharmacist					Follow -up
	Mini-cog	Animal Fluency	MMSE*	Clock-drawing test	3-item recall	
Breslow [133]		✓	✓	✓		X
Rickles [134]	✓	✓				✓
Setter [159]	✓**			✓	✓	X
Sonnett [152]	✓					X

**Mini-Mental State Examination; **Rapid 3-minute mini-cog consisted of the clock-drawing and 3-item recall*

Miscellaneous

The audit conducted by Manrai et al. [135] aimed to identify the variety of interventions provided to patients with dementia in a pharmacy setting and additionally how reliably information was documented. Interestingly, the majority of interventions in this audit were conducted by pharmacy technicians rather than a pharmacist.

A very different intervention is reported by Anderson et al. [151]. This study comprised of three visits from a pharmacist to patients, where their cognitive function was assessed by use of the medi-cog. As part of this assessment, the patient's ability to fill and use a pillbox were examined. It is not clear precisely how many patients in this study had a diagnosis of dementia but in recognition of the results it is estimated to be greater than 70%.

2.5.2.7 *Outcome measures*

The large range of outcome measures are presented in their humanistic, process, clinical, and economic categories as well as by their intervention category.

Medication Reviews

Humanistic Outcomes

Five of the medication review based studies included humanistic outcome measures. Furniss et al. [145] recorded the number of falls and deaths; Kröger et al. [148] recorded the levels of agitation and comfort; Fountain et al. [144] recorded the risk of falls; Paquin et al. [157] recorded numbers of hospital readmissions, admissions to emergency departments and levels of mortality 60 days post intervention. D'Souza et al. [158] recorded measurements of ADL, Modified Caregiver Strain Index and Agitated Behaviours in Dementia Scale.

Process Outcomes

Table 13 summarises the process outcomes for the 13 medication review studies. Fifty percent of the studies has process outcomes relating to a change in the number of prescribed medicines whilst D'Souza et al. [158] had more specific outcomes which included dementia management quality measures.

Table 13. Medication Review: process outcomes

Author	**Process measures**					
	Number of prescribed drugs	Adherence and awareness	Number of med. changes	Number of interventions	% accepted	Intervention type
Collier [136]		✓				
Conlon [137]	✓					
D'Souza** [158]						
Farrell [156]	✓	✓				
Fountain [144]	✓	✓				
Frausto [154]	✓			✓		
Furniss [145]	✓					
Gustafsson [160]	✓			✓		✓
Kröger [148]			✓			
Mouchoux [143]				✓	✓	✓
Paquin# [157]						
Patel [139]				✓		✓
Stuhec [140]	✓		✓		✓	

**Intervention(s); **Interventions do not fit under these categories. Process outcomes included Dementia management Quality measures and time taken for patient to be placed (i.e. into a nursing home); #Time of pharmacist call*

Clinical Outcomes

Four studies had clinical outcomes which included: baseline dementia severity [158]; state of delirium, AD progression, presence of leg cramps [144]; the names of main medicines involved in the interventions [143] and MMSE, Geriatric Depression Scale (GDS), Brief Assessment Schedule Depression Cards (BASDEC) and Crichton-Royal Behaviour Rating Scale (CRBRS) scores [145].

Economic

Paquin et al. [157] was the only study in this category to report any economic aspect which in this case was a cost analysis comparing the readmission costs to Veterans Affairs Medical Canter with and without the Pharmacological Intervention in Late Life (PILL) service.

Targeted medicine intervention

Humanistic

Three humanistic outcomes were recorded from the seven studies in the targeted medicine intervention category: Caregiver burden [149], Quality of Life and ADL [150].

Process

Table 14 summarises the types of process outcomes reported by the 7 studies. Most revolved around the number of prescribed medicines and the reduction in medicines reported and number of interventions.

Table 14. Targeted Medicine Intervention category, process outcomes

Author	**Process measures**				
	Number of prescribed drugs	Reduction in medicine	Number of interventions	Chronic Care measure 10.1	Intervention type
Cations [141]		✓*			
Child [162]	✓	✓*	✓		
Efjestad [153]	No outcomes reported				
Hursh [147]	✓			✓	
Nakamura [149]	No outcomes reported				
Maidment [138]			✓		✓
Sakakibara [150]	✓	✓**			

**Reduction in regular antipsychotics; **Reduction in benzodiazepines*

Clinical

Nakamura et al. [149] assessed dementia severity and swallowing function whilst Efjestad et al. [153] assessed ADS scores and determined the most common ADS medicines that were prescribed.

Economic

No studies in this category reported any cost related outcome measures.

Education

Humanistic

A variety of humanistic outcomes were recorded in this category including: frequency of disruptive behaviour and number of stressful events [146]; level of understanding [155] and the patient's ability to find support [142].

Process

Monette et al. [146] reported the proportion of discontinued psychotropics or dose reductions and the proportion of other psychotropics being used. Watanabe et al. [155] measured medication persistence rates and reasons for discontinuation whilst the PCN report [142] evaluated and reported on the effectiveness of the PCN training programme and the PCN role.

Clinical and economic

No clinical or economic outcomes are reported for these categories.

Memory Screening

Humanistic

Outcomes included: patient satisfaction [134]; mean responses to survey statements [133]; associations between mean Charlson Comorbidity Index scores (to assess comorbidity burden) and mean problem index with mini-cog scores [159] and the proportion of participants requiring assistance according to a questionnaire and the associations of the findings with mini-cog scores [152].*Process*

Rickles et al. [134] was the only research study to report a process outcome which was the proportion of patients referred to a GP and from the proportion that were referred, how many actually visited their GP.

Clinical

Table 15 summarises the clinical outcomes, which are all (as expected) memory based.

Table 15. Memory screening category, clinical outcomes

Author	Clinical Outcome
Rickles [134]	Proportion found to have a cognitive deficiency
Breslow [133]	Mean MMSE* Percentage that scored 17 in the category fluency test Mean clock draw score
Setter [159]	Proportion to pass/fail the mini-cog
Sonnett [152]	Proportion 'suggesting cognitive impairment' Number of new Alzheimer's Disease diagnoses

**Mini-Mental Score Examination*

Economic

Rickles et al. [134] reported the participants willingness to pay in their research. No other studies in this category reported cost related outcome measures.

Miscellaneous

Humanistic

No humanistic outcomes measures were reported by either Manrai et al. [135] or Anderson et al. [151].

Process

Due to the nature of the research, Manrai et al. [135] reported several process outcome measures which included:

- Number of interventions
- Types of interventions
- Frequency and quality of documentation
- Time spent conducting interventions and resolving issues from the interventions

Clinical

Anderson et al. [151] reported the following clinical outcome measures:

- Mean (SD) medi-cog score (0-10)
- Mean (SD) Pillbox Fill (PBF) score (0-1)
- Mean (SD) Prospective Pill Count (PPC) score (0-1)
- PBF and PPC pass rates

- Correlation coefficients

2.5.2.8 *Outcome results*

Humanistic and Process

A wide range of results from a wide range of outcome measures were reported across the 29 studies. Tables 16-17 summarise the key humanistic and process outcome results from each study in the first 4 categories: Medication review, targeted medicine intervention, education and memory screening.

In regards to the miscellaneous category, Anderson et al. [151] reported no humanistic or process outcome measure results but Manrai et al. [135] reported the following process outcome results:

- Total of 102 interventions
- Least recorded piece of information was 'person intervention was discussed with' (55%)
- Most common interventions were: Dose alteration (16.7%) and delivery date confusion (15.7%)
- 87.2% interventions were conducted by a technician
- Total time spent on interventions was 1257 minutes

Table 16. Humanistic and process outcome results

Author	Humanistic results	Process results
		Medication review
Collier [136]		• Total number increased from 6.0 to 6.8 per patient but remained lower compared to pre-intervention (7.1) • Psychotropic medicines fell from 2.3 to 1.7 to 1.35
Conlon [137]		• Reduction in average number of medicines (7.1 to 6, p<0.003), psychotropics (2.3 to 1.7 (p<0.002) and antidepressants (0.7 to 0.2 (p<0.001)
D'Souza [158]	• Baseline: COACH* had high level of behavioural disturbance, functional impairment and high levels of caregiver strain	• No true results yet as still enrolling but program aligns with 9/10 DMQM** process measures. • Mean time to placement: Intervention (n=24): 29.6± 14.3 weeks, Control (n=5): 29.6 ± 14 weeks, (p=0.99)
Farrell [156]		• Medication list reduced from 27 to 20 • Pill burden reduced from 29 pills/day to 14 pills/day • 4-times/day reduced to twice daily dosage • Improved medication awareness and adherence
Fountain [144]	• Patient had more free time and happier • Clutter reduced and hazards removed • Risk of fall reduced	• Nurse filled weekly pill box and adherence improved
Frausto [154]		• Inpatient recommendation (n=37): discontinue unnecessary medicines (32%) • Outpatient recommendations (n=17): improve communication between inpatient team and primary care provider regarding medicine usage/monitoring (29%), ensure medication received at discharge (23%) • Total number of outpatient medicines did not differ compared to admission (15.4 vs 15.7 p=0.32)
Furniss [145]	• Fewer deaths (4 vs 14) in intervention homes (p=0.028)	• 54% of neuroleptic prescribing was deemed inappropriate • 144 actual treatment changes
Gustafsson [160]		• 1758 actions • Anticholinergics: 72 (8%), [59 (6.6%)], p=0.003. • Benzodiazepines: 80 (8.9%), [65 (7.3%)], p=<0.001 • Antipsychotics: 179 (20%), [160 (17.9%)], p<0.001 • Stop drug therapy and reduce dosage =most common
Kröger [148]	• Levels of agitation and comfort did not change noticeably	• 'Some' changes in medication observed
Mouchoux [143]		• 190 interventions from 560 orders • 77.9% accepted • Main problem: non-conformity to drug preference (39.9%) • Drug groups involved in most interventions: Nervous system (32.1%); gastrointestinal (22.6%) • Average analysis per patient = 16 minutes
Paquin [157]	• Readmittance = 25% (intervention), 37.1% (C1***), 34% (C2) • Intervention significantly lowered likelihood of readmittance than C1 (OR 0.72 [0.57-0.91)	• Adjusted analysis found that each additional 5 minutes of call time was associated with 15% lower likelihood of 60-day readmission (OR 0.85, 0.75-0.97)
Patel [139]		• 95% patients needed a pharmacotherapeutic intervention (30% medicine for no indication, 12% providing education, 10% discontinuing anticholinergic drugs, 10% enhanced adherence
Stuhec [140]		• 51% had (mainly dose adjustment) suggestions made to GP • 70% were accepted by GP • Reduction in inappropriate prescribing reduced from 20 to 6

**Caring for Older Adults and Caregivers at Home program; **The Dementia Management Quality Measures – this consists of 10 clinical performance measures intended to define optimal dementia care and guide quality improvement such as 'Cognitive assessment' and 'Counselling regarding safety concerns'; ***C1 (Comparison 1) is where patients were not reached by a telephone call and C2 is where they were reached but did not engage and the call lasted ≤ 5 minutes*

Table 17. Humanistic and process outcome results - continued

Author	Humanistic results	Process results
	Targeted medicine intervention	
Cations [141]		• 54/81 participants have commenced deprescribing and 49/54 have achieved cessation • 26.5% of the 49 recommenced an antipsychotic due to BPSD* recurrence
Child [162]		• Antipsychotics reduced/withdrawn=43 (61.4%) in 13 practices • Most commonly prescribed: Amisulpride (32.3%), Risperidone (23%), Quetiapine (21.7%)
Efjestad [153]	**None reported**	
Hursh [147]		• Antipsychotic prevalence reduced from 40.5% (1.5.08-31.8.08) to 21.6% (1.3.09-30.6.09)
Maidment [138]		• Medication discontinued/ dose reduced (n=11) [4=Lorazepam, 1=zopiclone] • No action taken (n=6)
Nakamura [149]	• Mean J-ZBI_8** score for personal strain reduced from week 0 to week 4 (p<0.05) through to week 16 (p<0.01).	
Sakakibara [150]	• Benzodiazepine reduction group had ADL# mean [SD] difference from baseline to 6 months (14 [11.1], (specifically including walking and bladder control) p<0.01) and QOL## mean [SD] difference from baseline to 3 months of 0.13[0.21], p<0.05	• Mean [SD] number of prescribed drugs significantly reduced from 7.1 [2.3] to 4.5 [2.1] (p<0.01) by 3 months in intervention group
	Education Interventions	
Anonymous [142]	• Support from pharmacy after Primary Care Navigator intervention increased from 2.81 to 3.38 (5=easy)	• Training increased confidence in dementia interaction
Monette [146]	• Mean NHBPS^ scores decreased from 16.3 at T1 to 11.4 by T6. • ANCOVA^^ showed significant effect of the intervention (p<0.0001)	• 61 (75.3%) attempts for discontinuation/dose reduction by T6 • 40(49.4%) discontinuations
Watanabe [155]	• Non- Donepezil Outpatient Consultation Service (DOCS) discontinuation reasons: transfer to another hospital (n=11), side effects (n=9)	• Average duration of treatment: 248.6 ± 184.1 days (non-DOCS) and 379 ± 202.6 days (DOCS) • Higher 1-year medication persistence rate in DOCS (73.1% vs 49.2%), p=0.01) • DOCS discontinuation reasons: transfer to another hospital (n=9), side effects (n=3)
	Memory Screening Interventions	
Breslow [133]	• Correlation between 'offering screening in community pharmacy is a good idea' and 'is convenient' (p=0.004) • 'It is a good thing to have my memory tested': Mean [SD] = 4.62 [0.57]	
Rickles [134]	• 74 (46%) completed voluntary survey of which 98.6% were 'very satisfied'/ 'satisfied' with the program	• 54 (33.5%) were referred • An additional 8 were referred based on clinical judgement • 23(69.7%) went/planned to go to the doctor
Setter [159]	• No difference in mean Charlson Comorbidity Scores (p=0.60) • Screen fail group had greater problem index (1.35 ±0.86 vs 1.07 ±0.56) but probability of association with mini-cog did not exceed what expected by chance (p=0.21)	
Sonnett [152]	• Higher proportion needed assistance with their medicines if more likely impaired (n=13, 39.4% vs n= 42, 15.7%)	

**Behavioural and psychological symptoms of dementia; **Japanese version of the Zarit Caregiver Burden Interview; #Activities of Daily Living; ##Quality of Life; ^Nursing Home Behaviour Problem Scale (identified 29 potential behaviours that could lead to the prescribing of antipsychotics or use of restraints; ^^Analysis of covariance*

Clinical

Only 11 studies (38%) reported any clinical outcome measures with several relating to the stage of dementia. Table 18 lists these studies and their results.

Table 18. Clinical outcome measure results from each category

Author	Clinical results
	Medication Review Interventions
D'Souza [158]	• Mean (SD) Mini-Mental State Examination (MMSE) score was 16 ±6 in both intervention and control
Fountain [144]	• Anticholinergic agents discontinued and furosemide changed from evening to morning dose • Thyroid levels increased dose reduced • Memantine added and MMSE score increased from 14 to 19 • Night incontinence stopped • Gemfibrozil stopped and leg cramps resolved
Furniss [145]	• No significant results in changes in assessment results or recorded falls.
	Targeted medicine Intervention
Efjestad [153]	• 24/50 participants concurrently used anticholinergic drugs • Where Anticholinergic Drug Scale (ADS) score was ≥2, median score reduced from 2.5 to 1.0 (p=0.009) after intervention • Tolterodine (ADS=3), n=2, • Escitalopram (ADS=1), n=7, • Prednisolone (ADS=1), n=6
Nakamura [149]	• 20/27 patients showed at least one-stage improvement in severity • Patients with impaired swallowing function at week 0 had a significantly improved RSST** score at all time points (all P<0.05)
	Education Interventions
Watanabe [155]	• Mean [SD] score for understanding increased from 2.5 [1.7] to 5.7 [0.7], p<0.001
	Memory Screening Interventions
Breslow [133]	• MMSE mean= 28.8 • Category fluency (number of animals stated in 60 seconds): 92.3% ≥17 • Clock draw mean= 3.92 and 92.3% answered correctly 4 of 4
Rickles [134]	• 71 (44.1%) had at least one cognitive deficiency
Setter [159]	• 17% failed mini-cog (scores 0-2)
Sonnett [152]	• 55 (18.3%) 'likely impaired' • 5 patients evaluated by neurologist, diagnosed with Alzheimer's Disease and commenced Acetylcholinesterase Inhibitors
	Miscellaneous Interventions
Anderson [151]	• Mean (SD): Medi-cog= 3.8 (1.5); PBF*= 0.78 (0.29); PPC**= 0.80 (0.30) • % pass: PBF= 59.4; PPC= 67.2 • Medi-cog vs PBF correlation= 0.668; Medi-cog vs PPC correlation= 0.660 (both p=<0.01)

**Pillbox Fill; **Prospective Pill Count*

Economic related outcome measure results

Two studies (Furniss et al. [145], Paquin et al. [157] reported any economic related outcome measure results. The trend tended to be positive and in favour of a pharmacist-based intervention and the results are detailed in Table 19.

Table 19. Cost related outcome measure results for all categories

Author	Economic results
Furniss [145]	• Trend for reduction in costs in intervention group
Paquin [157]	• Pharmacological intervention in Late Life (PILL) programme saved $804 per participant in readmission cost [C1]* and $537 [C2]* • Net saving between $138,134 and $206,696
**C1 (Comparison 1) is where patients were not reached by a telephone call and C2 is where they were reached but did not engage and the call lasted ≤ 5 minutes*	

2.5.2.9 *Effective elements*

There were 72 effective elements identified from the studies which were later broadly categorised as summarised in Table 20.

The use of a pharmacist in the intervention and the involvement of MDTs were common elements of the studies to be reported as being a contributing factor to their success.

Training related elements included how it included the training of non-professionals [142, 151], the intervention utilised existing skills [139, 145], improved current skills [142] and was simple and minimal training [133, 152].

For Anderson et al. [151], Breslow [133] and Rickles et al. [134] tool related elements involved the use of a simple and quick tool being used.

The involvement of or benefit to patients and their families in the intervention were also reported by several of the authors such as the intervention being customised for each patient [157] and the intervention improving patient safety/care/QOL/health outcomes [142, 149, 152, 157, 158].

Other effective elements included D'Souza et al. reporting how their intervention deemed valuable to stakeholders [158] and Anderson et al. [151], Rickles et al. [134] and Watanabe et al. [155] reporting how their intervention model would be replicable in other settings.

Table 20. Effective elements identified from studies

Author	MDT[1]	Accessibility[2]	Training[3]	Cost[4]	Tool[5]	Patient/family[6]	Other[7]
Cations [141]	✓						
Child [162]	✓						
Collier [136]	✓						
Efjestad [153]	✓						
Farrell [156]	✓						
Fountain [144]	✓					✓	
Frausto [154]	✓						
Furniss [145]	✓		✓	✓	✓	✓	
Gustafsson [161]	✓						
Kröger [148]	✓						
Maidment [138]	✓						
Monette [146]	✓		✓				
Mouchoux [143]	✓						
Nakamura [149]	✓					✓	
Paquin [157]	✓	✓		✓		✓	
Patel [139]	✓	✓	✓				
Sonnett [152]	✓	✓	✓	✓	✓	✓	
Stuhec [140]	✓						
Watanabe [155]	✓						✓
Anderson [151]			✓	✓	✓	✓	✓
Anonymous [142]		✓	✓			✓	
Breslow [133]		✓	✓		✓	✓	
Conlon [137]			None reported				
D'Souza [158]						✓	✓
Hursh [147]			✓				
Manrai [135]			None reported				
Rickles [134]		✓			✓	✓	
Sakakibara [150]			None reported				
Setter [159]			None reported				

[1] Authors reported including pharmacist or use of MDT enhanced service.
[2] Intervention easily accessible by patient
[3] Included training methods, improvement of current skills, use of peer and supervisor support and range of people who could be trained.
[4] Low cost or may reduce costs or resources currently used.
[5] Tool being described as simple, being quick to use or had high specificity and sensitivity
[6] Included intervention improving patient safety, health outcomes, patient satisfaction, facilitate engagement with family members
[7] Intervention able to be replicated or deemed valuable by stakeholders

2.5.2.10 *Ineffective elements*

Only 14 elements were explicitly reported by the authors as requiring further consideration for future trials of the intervention prior to successful implementation, due to potentially affecting either patient outcomes or the rigour of the study and these are listed in Table 21.

Table 21. Ineffective elements

Broad category	Author	Element requiring further consideration
Interpreting results	D'Souza [158]	Intervention did not lead to differences to time placements
	Anderson [151]	Results of assessment still need to be used prudently due to other patient factors
Patient identification	Child [162]	Identifying patient method using dementia register
	Breslow [133]	Intervention recruitment heavily relied on self-reporting in the first instance
	Anonymous [142]	Primary PCNs struggled to identify patients that may require support
		Difficulties raising awareness to public of new PCN role and service
Tool / intervention elements	Watanabe [155]	Ineffective timing of aspects of the intervention
		Lack of information provided to patient
	Breslow [133]	Poor sensitivity of tool for early cognitive changes
	Anderson [151]	The assessment was arduous to implement
Healthcare professional barriers	Rickles [134]	Communication issues between community pharmacists and physicians caused low patient follow-ups
	Anonymous [142]	Difficulties convincing GPs of potential benefits for the scheme and to get the GPs to embrace the scheme
		Training difficulties
		Lack of time to do role

2.5.2.11 *Quality assessment*

Table 22 summarises the overall quality of each paper based on the GRADE method and the areas where papers were downgraded or upgraded.

As it can be seen, eighteen of the studies were rated 'Very Low', six were 'low', two were moderate and one was rated 'High'. The score on GRADE only goes to 'VERY LOW', however due to the low quality study designs used for most of these studies (service evaluations), most studies began at a rating of 'LOW' (the default score for service evaluations). Therefore after two or more downgrading issues, several of the studies technically had a rating lower than 'VERY LOW' which has been using an asterix within Table 22.

Table 22. GRADE ratings of quality for each paper

Author	Category	Limitations	Inconsistency	Indirectness	Imprecision	Reporting Bias	Overall Quality of paper
Collier [136]	Medication Review	😐	😐	😐	☹	☹	VERY LOW*
Conlon [137]		😐	😐	😐	😐	☹	VERY LOW
D'Souza [158]		😐	😐	☹	😐	😐	LOW
Farrell [156]		😐	😐	😐	☹	😐	VERY LOW*
Fountain [144]		😐	😐	😐	☹	☹	VERY LOW*
Frausto [154]		😐	😐	☹	😐	😐	VERY LOW*
Furniss [145]		😐	😐	😐	😐	😐	HIGH
Gustafsson [160]		😐	😐	😐	☺	😐	MODERATE
Kröger [148]		😐	😐	☹	☹	☹	VERY LOW*
Mouchoux [143]		😐	😐	😐	😐	😐	LOW
Paquin [157]		☹	😐	😐	😐	😐	VERY LOW
Patel [139]		😐	😐	😐	☹	☹	VERY LOW
Stuhec [140]		😐	😐	😐	😐	☹	LOW
Cations [141]	Targeted Medicine Intervention	☹	☹	😐	☹	😐	VERY LOW*
Child [162]		☹	☺	😐	😐	😐	LOW
Efjestad [153]		😐	😐	😐	☹	😐	VERY LOW
Hursh [147]		☹	😐	😐	☹	😐	VERY LOW*
Maidment [138]		😐	😐	😐	☹	☹	VERY LOW*
Nakamura [149]		😐	😐	☹	😐	😐	VERY LOW
Sakakibara [150]		☹	😐	😐	☹	😐	VERY LOW
Anonymous [142]	Education	😐	😐	😐	☹	☺	LOW
Monette [146]		😐	😐	😐	☺	😐	MODERATE
Watanabe [155]		😐	😐	😐	☹	☺	LOW
Breslow [133]	Memory Screening	☹	😐	😐	☹	😐	VERY LOW*
Rickles [134]		☹	😐	😐	😐	😐	VERY LOW
Setter [159]		😐	😐	😐	☹	😐	VERY LOW
Sonnett [152]		😐	😐	😐	😐	😐	LOW
Anderson [151]	Miscellaneous	😐	😐	☹	😐	😐	VERY LOW
Manrai [135]		😐	😐	😐	😐	😐	LOW

Key: Initial score downgraded= ☹; Initial score stays the same= 😐; Initial score upgraded= ☺
**Final score technically lower than given score (0 is the lowest score you can downgrade to)*

Downgrades

The majority of downgrades were due to imprecision and Table 23 shows the reasons for each downgrade within this category.

Table 23. Causes for an imprecision downgrade

Author	Cause of imprecision downgrade		
	Small Sample Size	Other	Comment
Anonymous [142]	✓		
Breslow [133]	✓		
Cations [141]	✓	✓	Limited data
Collier [136]	✓		
Efjestad [153]	✓	✓	Small effect size
Farrell [156]	✓		
Fountain [144]	✓		
Hursh [147]		✓	No statistical tests done where able. Only reported percentages.
Kröger [148]		✓	Not specific with number reporting.
Maidment [138]	✓		
Patel [139]	✓		
Sakakibara [150]	✓		
Setter [159]	✓	✓	Does not meet sample size that power size calculation required
Watanabe [155]		✓	Wide confidence intervals

Upgrades

Only five studies had GRADE categories upgraded which are detailed in Table 24.

Table 24. Reasons for study upgrades

Author	Reason for upgrade
Anonymous [142]	Good reporting of limitations and minimal bias in the study.
Child [162]	Consistency within the research. One pharmacist conducted all 70 reviews.
Gustafsson [160]	Precise and high magnitude. Big sample size and effect size.
Monette [146]	Highly significant results proven with statistical methods.
Watanabe [155]	Good reporting of limitations and minimal bias in the study.

2.5.2.12 *Study limitations*

The limitations listed by the authors tended to not be exhaustive as other limitations were reported by R1 during this review. Appendix 5 shows the limitations reported by both author and reviewer.

2.6 Discussion

Key findings

The majority of the included studies were from the USA (34%) and the UK (24%) with most being service evaluations. Very few of the studies (25%) were conducted in primary care settings and recruitment to the studies was largely opportunistic with very few obtaining written consent nor involving a follow-up.

The interventions tended to use a multidisciplinary team and the majority of the interventions were medicines focussed with particular interest towards antipsychotics, anticholinergics and benzodiazepines.

The studies reported a wide range of process and humanistic outcomes and a variety of effective elements to their interventions with many being related to the use of a pharmacist or a MDT.

The overall quality of the research identified in this review was largely rated as 'low' or 'very low' with only 1 study (an RCT) being rated as high.

Strengths and limitations

This review had several strengths. The first was that prior to conducting this SR, a scoping review was completed. The scoping review highlighted several key issues with the proposed research question and screening procedure which ultimately led to very few results. The scoping review led to a broadening of the inclusion criteria which enabled many more relevant studies to be eligible for data extraction.

Reputable sources such as the Cochrane Handbook for SRs of Interventions [126] which provides detailed advice on: the standard methods to planning a review; searching and selecting studies; data collection; and assessing bias was used. This handbook provided the resources to conduct an objective SR which utilised methods that are well known and validated.

The quality of the research was also assessed using the GRADE [131] method, thereby enabling the results of the studies to be interpreted more accurately as any subjectivity from the authors reporting was scrutinized.

This review used two independent raters at each stage of the screening process. This reduced any risk of screening bias from R1 which could have affected the types of and number of studies to be included. It ensured that all studies met the inclusion criteria but simultaneously guaranteed that all possible studies were included.

Calculating the Cohen's Kappa at each stage of the screening process provides insight into how much disparity there was between the independent raters and how much selection bias could have been introduced.

Although the scoping review reduced the limitations in this study, several are still of note. Firstly, a large proportion of the studies selected were only available as conference abstracts which caused data extraction and quality analysis to be difficult and limited. This contributed to the majority of the studies included in this review being of poor quality.

Another limitation to this review was the second independent rater (R3) during the title screening stage was not a pharmacist and had no in-depth prior knowledge of our study aims. The 'fair' level of agreement seen at this stage reflected this as there was a clear difference between the raters regarding which studies would meet the inclusion criteria.

Although the number of search databases was increased in this review following the results of the scoping review, it is unlikely that every possible search avenue was utilised. This will have been a mixture of limited knowledge of other search possibilities by the researcher, limited subscriptions by the university and limited time and manpower to conduct an extremely large search.

The final limitation to this SR was regarding the data which was extracted. In this review, the training of staff members to conduct the interventions was not comprehensively documented or evaluated. This would have been an important aspect to evaluate in more detail as the effective training of staff will be paramount for the intervention to succeed and provide the service users with the best possible experience.

Study characteristics

Although the review included studies from any country, the results showed that over half of the studies were from the USA and the UK. In some ways this is not surprising as these are

two of the most prominent countries for conducting research. It is surprising however that countries such as Australia have not conducted more studies in this field considering their pharmacy roles are similar to the UK and have contributed research in other fields of pharmacy.

In terms of developing a new pharmacy intervention, the fact that several of the studies were based in the UK is an advantage because the interventions identified will have been tested within the same healthcare system using similar environments and HCPs with similar roles. This means that the results from the UK studies can be directly placed within the context of a future intervention which would be developed in the UK.

A range of study locations were reported in this review but only 25% of the studies were conducted in primary care. This may reflect the fact that this is a special group with complex needs and therefore expert input is required or a lack of expertise in dementia management in primary care. On the other hand, it may just reflect the fact that the area is simply under researched in primary care. The latter may partly be due to a general lack of awareness of the frequent close contact primary care settings (such as community pharmacies) are in close contact with people affected by dementia and how there is the potential to be more involved in their care.

This review included a vast number of service evaluations and only included one RCT. Although the service evaluations are not regarded as high quality studies, it was important to include them in this review as they still provided insight into how a pharmacist or a pharmacy could potentially play a key role in supporting PWD.

Due to many of the studies included in this review being service evaluations, recruitment methods tended to be opportunistic and did not require written consent. Once an intervention or tool has been developed and piloted on a small scale, the MRC [92] recommend that the intervention is tested for effectiveness and cost effectiveness. This requires preferably a large scale randomised controlled trial study design in order for a true effect size of the intervention to be determined. In order to be enrolled onto such a study, written informed consent would be a requirement, which determining on the level of dementia, could be a barrier difficult to overcome and would need considerable thought before such a study could be conducted.

Very few other recruitment methods were utilised in the studies but included study promotion via posters or word and mouth and referrals to join the study via health

professionals. The limited recruitment methods recorded means that studies targeted at other groups of patients (for example asthma or diabetes) may need to be sought prior to developing a study testing a new intervention in order to gain a wider range of methods which may be more effective and appropriate to the target participants. Additionally, further work into the recruitment methods of other studies may provide clues as to how the intervention (if successful in the studies) would be promoted and service users referred to the service.

Very few studies had any long-term follow-up after their intervention which means that the ongoing benefit to patients has not been considered and that the positive results reported in the studies have unknown long-term benefit. The lack of follow-up is probably a repercussion of the types of studies that were included in the review. As already mentioned, many of the studies were small-scale service evaluations which can cause follow-ups to be difficult either because of funding or recruiting issues. This is an element which will require some thought when designing a study to test the developed intervention. This is because it is important to assess both the short and long-term benefits to the service-users, as this may have consequences for the viability and cost-effectiveness of the intervention.

Types of interventions

The majority of the interventions were unsurprisingly medication related, with many of the studies concentrating on antipsychotics, anticholinergics and benzodiazepines. The fact that these medicine groups are being targeted in PWD is not surprising because as mentioned in section 1.5.2, antipsychotics are linked to an increased risk of cardiovascular events and death when prescribed to PWD [163] and anticholinergics along with benzodiazepines further reduce the levels of acetylcholine in the body leading to heightened confusion and risk of delirium and falls [164].

Although most, if not all, community pharmacies already offer medicine use reviews (as mentioned in section 1.9, which would encompass those taking antipsychotics, anticholinergics and benzodiazepines, there is a stipulation that at least 70% of the reviews carried out annually must be with patients [90]:

- Prescribed high risk medicines (NSAIDs, anticoagulants, antiplatelets and diuretics)
- Recently discharged from hospital with changes made to their medicines

- Diagnosed with respiratory disease
- At risk of or diagnosed with CVD and regularly being prescribed at least 4 medicines

This means that although community pharmacists are trained to conduct a more general review of a patient's medicines and are compensated financially for doing the reviews, there is currently no training or emphasis on seeking potential issues with the use of antipsychotics, anticholinergics or benzodiazepines, and in particular, in PWD.

The results from this review, however, emphasise the need for the developed intervention to include an element which pays particular attention to the medicines (such as antipsychotics, anticholinergics and benzodiazepines) which have the potential to cause greatest harm to PWD.

A memory screening service was another type of intervention which was featured in this review. Although a memory screening service on the surface seems like a viable option for community pharmacies to undertake as minimal training would be required, would not take up an excessive amount of time and pharmacists may be enthusiastic to improve their clinical knowledge in the area and learn a new skills, the larger picture needs to be considered. As mentioned in section 1.9, GPs are incentivised to reach certain targets. GP surgeries currently receive QOF points for:

- Establishing and maintaining a register of patients diagnosed with dementia
- Reviewing 35-0% of patients diagnosed with dementia whose care plan has been reviewed in face-to-face review in the preceding 12 months [106].

If a pharmacy were to conduct the memory screening, there would have to be careful thought as to what the care pathway would look like for the patient because for the service to be accepted by all HCPs, GP surgeries would have to be included in the service to ensure that there is no detriment to receiving their QOF points.

The Primary Care Navigator evaluation report [142] offered signposting as part of their intervention which was reported to be of great benefit to people affected by dementia in the community. As mentioned in chapter 1, signposting is already an essential service for community pharmacies [90] but is often underutilised. This can be due to a lack of awareness of the local services available to the community and a lack of training or resources for the primary care staff. The latter was reported in a qualitative study which explored the experiences and views of community pharmacy staff in relation to current practices of managing OTC medicine abuse (n=17). The study found that many of the

participants (pharmacists and pharmacy assistants) appeared uncertain of referral options and concluded that improved knowledge for community pharmacy staff about signposting to relevant services was needed [165]. A developed intervention could therefore aid the provision of this essential service by including up-to-date and thorough signposting for local or more national dementia and carer related support services.

Study outcomes

The wide range of services captured in this review understandably led to a wide range of reported outcome measures. The majority of outcome measures were categorised as either process or humanistic, with fewer being clinical outcomes and only 1 study reporting an economic outcome.

With the majority of interventions being related to the prescribed medicines of participants, it is logical that process outcome measures were the most common category. It was reassuring that several studies considered humanistic outcome measures as they are an important aspect to consider in the design of an intervention targeted towards people affected by dementia.

When testing the intervention, a humanistic outcome measure which should be considered is patient satisfaction. Patient satisfaction is becoming increasingly important for the financial performance of healthcare providers for patient well-being [166]. The high satisfaction results reported by Breslow [133] reinforces the idea that community pharmacies are well placed for interventions and that patients could be receptive to visiting their pharmacy for an ever growing range of healthcare services. A robust measure of patient satisfaction should therefore be incorporated into the evaluation of the developed intervention in order to confirm whether it would be accepted and used by the target population.

Positive economic trends were reported (although only by three studies), which provides a foundation that further research into an intervention targeted at those affected by dementia may not only be of benefit to service recipients, but may also provide savings to the NHS in the long term from potential reduced hospital admission rates. Positive economic trends have been reported for other pharmacy-managed services such as those included in a systematic review (n-25) which targeted people with diabetes mellitus where cost savings when compared to usual care ranged from USD$8 to USD$85,000 per person per year [167]. For an intervention to be successful, it must show cost-effectiveness which

involves the use of economic outcome measures during large, high quality studies. The much larger number of studies which were selected for the diabetes systematic review which included economic outcomes (n=25) reinforces how little research there currently is regarding dementia services pharmacy settings that involve economic data. Studies in this area should therefore begin using economic outcome measures alongside the process, humanistic and clinical outcome measures in order to improve the quality of the studies and likelihood of the intervention being implemented.

Effective and ineffective elements

Out of the seven identified effective elements, the three most common aspects reported were the use of an MDT involving a pharmacist, the training provided and the benefits to or the involvement of the patient or family member.

With the speciality knowledge that pharmacists are equipped with and their increasing use in a variety of settings, it is not surprising that many of these studies identified the incorporation of a pharmacist within their intervention as being an asset. Additionally, these studies have not only reinforced how versatile and of benefit pharmacists can be to PWD, but also provides further evidence for how the use of a MDT (which was also commonly used in these studies) can enhance the care of PWD. These studies did not report how well the different HCPs interacted with each other however and this is another aspect to be considered in future studies and a future intervention to ensure that the patient care journey is never compromised. The benefits of using MDTs has also been reported in other health conditions. Head and neck MDT meetings saw 52 patients (30%) have changes made to their management of which 20 (67%) were classed as major [168] and HCPs involved in cancer care reported multiple benefits to MDT meetings such as more accurate treatment recommendations, MDT evaluation and adherence to clinical guidelines [169]. These results reinforce how the use of MDTs are becoming more mainstream and often have significant benefits to both the HCP and the patient. The intervention should ensure that a variety of HCPs are included (where possible and is dependent on the type of intervention) to ensure that the patient has optimal care.

Although training was not an area which was documented during data extraction, this aspect being a popular effective element raises awareness to how this is an important area to think about during the design of an intervention. Primary care settings can be busy places with high, stressful workloads and long hours and this needs to be considered during the design of the required training. The training provided in the PCN study [142] showed

how a variety of methods (such as study days, e-learning and ongoing mentoring) can be used to accommodate different learning styles and can be used in a way to cause minimal extra workload and pressure to the staff but still ensure that required the learning takes place. The types of teaching methods used would also be easily reproduced, which would enable the intervention to be transferrable across the UK to have a higher impact.

Key points to consider in regards to the training required for the intervention, highlighted by the studies that identified training related effective elements include:

- Who should be trained?
- What knowledge should be learnt?
- How should the training be delivered?
- How long should the training last?
- Should training be remunerated?
- How will the training be evaluated?
- How will the competency of the HCPs being trained be assessed?

Patient's participation in decision making in healthcare is becoming a political necessity in many countries and healthcare systems worldwide [170] and it has been associated with improved treatment outcomes in such conditions as diabetes [171] and depression [172]. The fact that some studies saw the involvement or customisation of the intervention dependant on the patient as an effective element enhances the idea of how patient participation should be considered when designing a future intervention and thought should be placed on precisely how it may improve patient related outcomes which could be rigorously tested in high quality studies.

Another effective element that surfaced was the simplicity of the intervention design and tool. This is an important factor to consider when designing an intervention for use by pharmacists if you are aiming for it to be easily reproduced nationwide and to ensure all points are covered each time by each pharmacist. The intervention therefore needs to be simple in concept and make use of standardised and clear frameworks. An example of this was identified with Paquin et al. [157] who used a structured medication review checklist (see Table 25) which assessed for potential drug related problems and medication discrepancies. The designing of a tool such as Paquin et al.'s would however need to be designed with care as it must be remembered that each patient seen during an intervention is different and may not conform to a simple checklist. There must therefore be room for manoeuvre within the tool that is designed in order to accommodate this.

Table 25. Medication review checklist tool used by Paquin et al.

	Potential drug related problems noted as follows:	
1	**Potentially Inappropriate Medications** [ ] Contraindication [ ] Drug without indication [ ] Beers criteria* [ ] Anticholinergics	**Anticholinergic Risk Scale Score** [ ] Ineffective agent [ ] Dosing [ ] Duplicate
2	**Interactions** [ ] Drug-Drug [ ] Drug-Disease	
3	**Adverse drug reactions** [ ] None identified	
4	**Polypharmacy & complex regimen** [ ] Considerations for streamlining	
5	**Medication discrepancies** [ ] Omission from discharge plan [ ] No active order (order omission) [ ] Active order for discontinued medication [ ] Dose, frequency, directions [ ] Other	**Identified during interview:** [ ] Patient taking differently than prescribed [ ] Patient taking extra medication not documented [ ] Patient not taking an active medication

**Criteria for potentially inappropriate drug prescribing in ambulatory older adults aged 65 years and over. This tool can be used to assess the quality of prescribing in older persons* [173]

Quality

Although a respectable number of studies were included in this review, they were largely graded as 'Low' or 'Very Low' quality. This was due to the fact that the majority of the studies were not randomized controlled trials by design which automatically places the studies at 'Low' and therefore required aspects worthy of upgrade which was only seen by 5 of the studies.

A large factor for studies to be downgraded was imprecision and this was fundamentally due to the small sample sizes seen in the small observational studies and consequently wide confidence intervals and underpowered results. This reinforces how future research in this area requires larger randomised controlled trials in order to truly test the effectiveness of the interventions.

Studies were also downgraded due to severe limitations in their study designs. Rickles et al. [134] used a voluntary survey to assess patient satisfaction with the service which could have led to social desirability bias as those who were satisfied with the service are more likely to want to leave positive feedback whereas those who had a negative experience may not feel so inclined. Particularly if the pharmacist is present in the room at the time of providing the feedback. Additionally, the questions regarding the patients' willingness to pay may be subjective dependant on the patients' social or economic status or age. Furthermore, the possible answers to the questionnaire are limiting for the patient so true

accounts of their thoughts may not be captured. Rickles et al. [134] also introduced high levels of recruitment bias as the recruitment was through the self-referrals of patients and via assessment for suitability by the pharmacist conducting the intervention. The questions raised by assessing the quality of the study by Rickles et al. [134] has highlighted further areas which need thought when designing a study to test the developed intervention. This includes: what any training to staff is comprised of; how participants are recruited avoiding recruitment bias; and how cost-effectiveness and patient satisfaction are objectively measured.

Although the overall quality of the studies were poor, one positive aspect was that all 29 studies used objective measurements and mostly validated tools such as the use of OBRA guidelines [138], mini-cog [159], ADS [153] and drug burden index [141]. These measures are well tested in other studies and provide some reliability and specificity to the results. Additionally, the use of objective measurements reduced the risk of interviewer bias or reporting bias as there is limited subjective input.

2.7 Chapter conclusions and logic model development

This review has highlighted how although there have been a variety of interventions tested in PWD, few have been conducted in primary care settings and even fewer were of high quality. This means that although this study has provided a wealth of possibilities for a future intervention, there is limited evidence of the effectiveness of the models included within this chapter or the ability to reproduce on a large scale, particularly within community pharmacy. The majority of the interventions involved a medication review or the targeting of particular medicines, particularly anticholinergics, antipsychotics and benzodiazepines and utilised a MDT which are factors which should be considered when designing a future intervention. These particular aspects have therefore been placed into the developing logic model (Figure 8). Effectively and actively signposting was also considered an element which could be included in a future intervention and has consequently been placed into the model. Authors also reported several effective elements which should be considered, particularly in a community pharmacy environment where time is not a luxury. Therefore, the effective elements of being time efficient, using varied training, being replicable in other pharmacies and using a tool such as review guide have also been added to the logic model.

Another effective element which was reported was that of including the patient in the intervention. As patient centred care becomes increasingly of importance in all healthcare settings, this was another element which needed to be included in the model.

All of these elements would need further research to determine their true effectiveness within a new intervention model due to the lack of high-quality evidence currently available. Additionally, several of the studies will have only included some of the elements in the logic model and so they're combined effect and ability to be implemented would also need to be determined regardless of previous evidence.

Although memory screening in community pharmacies is a novel idea which tended to have positive results, this study is about enhancing the medicines management of PWD, and although a memory screening service may aid to early diagnosis of dementia in the community, the intervention would have no scope for optimising their medicines management and may also be disregarded by general practice due to conflicts with QOF (as explained in section 1.9). Memory screening as a potential intervention type have therefore not been included within the logic model.

2.8 Next steps

Now that it has been identified what types of interventions have already been tested in pharmacy settings and from these, which may be of use in a future intervention for use in community pharmacy (such as some kind of medicine review based intervention), the next steps are to further identify what other content the intervention may entail which would be most beneficial specifically to PWD.

As described in section 1.6.2, pneumonia is a large cause of hospitalisation, cognition deterioration and death in PWD. Many potential risk factors for pneumonia have been identified, but not necessarily in a dementia cohort, which may have the potential to be reduced in a community pharmacy setting. The next chapters therefore aim to determine whether there are associations between some of the risk factors identified in section 1.6.2 and pneumonia for PWD and their potential inclusion in a future community pharmacy intervention, building upon the models identified in this chapter.

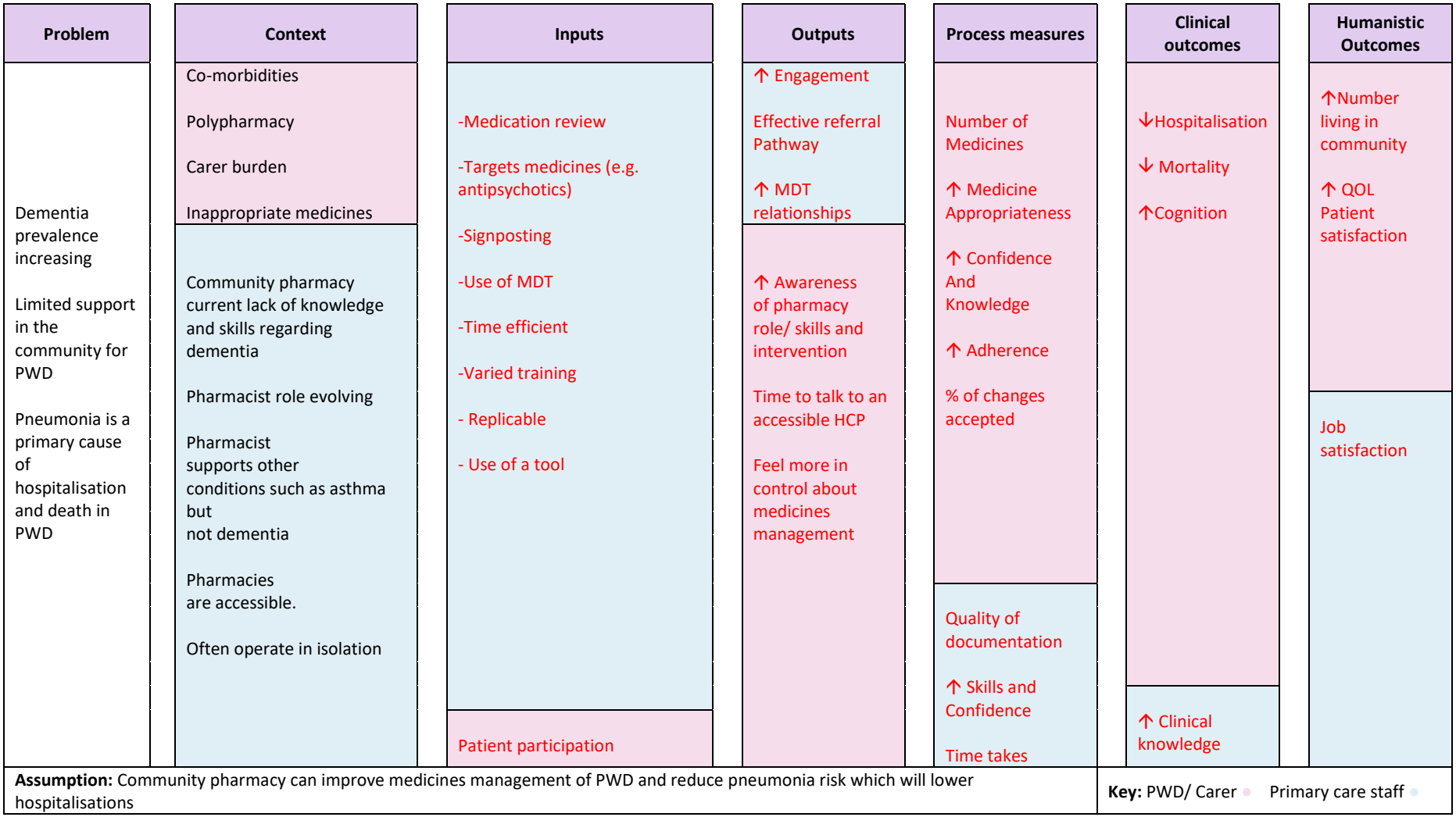

Figure 8. Developing logic model after SR

Chapter 3.

Prospective analysis of ward admissions

3.1 Chapter Overview

The results of the systematic review in Chapter 2 confirmed that there has been minimal research into interventions targeted at PWD within primary care but from those which have been conducted, various models had been tested which included a range of elements, with a basis of medication review being popular. The following chapters now concentrate on building on this basis by identifying and evaluating further elements which could be 86beneficial to PWD in a community pharmacy intervention aimed towards enhancing medicines management.

This chapter describes the rationale for a future case-controlled study and the initial work which was conducted within a local hospital connected to the university to test the feasibility of such a future study being conducted within a secondary care setting.

3.2 Introduction

Section 1.9.2 identified a number of risk factors which may be associated with an increased risk of developing pneumonia and therefore hospitalisation and mortality in PWD.

One way to enhance the medicines management of PWD is to reduce the risk of developing such a devastating complication in dementia (pneumonia) which in turn may reduce the risk of hospitalisation, which is known to cause an increased risk of delirium in PWD and lead to disorientation, increased mortality and morbidity on discharge [77]. To effectively develop a future intervention to be of value to PWD, it is therefore necessary to determine whether the identified risk factors are indeed associated with an increased risk of developing pneumonia, specifically in a cohort of PWD.

3.2.1 Future study

Study Design

There were a variety of study designs which were considered to explore the association of potential risk factors and pneumonia in a future study.

Longitudinal cohort studies (which can be prospective or retrospective) can be used to follow a cohort of participants over a period of time and analyse the cohort for patterns and trends. Nguyen et al. [174] used such a design to identify the long-term predictors of death from pneumonia in a general Japanese population. This study (n=9,462) had a long period of follow-up (29 years) and calculated hazard ratios for those who died from pneumonia when compared to those who did not.

Some advantages of longitudinal studies include being able to identify and relate events to particular exposures and further define the exposures with regards to presence and timing, the ability to follow changes over time in particular individuals within the cohort, it can exclude recall bias in participants (when done prospectively). Disadvantages include the incomplete and interrupted follow-up of individuals (particularly if there is a long period of follow-up), the potential for inaccuracy in conclusion if adopting statistical techniques that fail to account for the intra-individual correlation of measures and the general increased temporal and financial demands associated with this approach [175]. The temporal and financial demands associated with a longitudinal study, particularly a longitudinal prospective study, are the main reasons why this study design would not be feasible to explore the potential risk factors associated with pneumonia in PWD.

Randomised controlled studies are the most rigorous way of determining whether a cause-effect relation exists between treatment (or a specific intervention) and outcome but their use is limited by ethical and practical concerns [176]. In the case of our research question, this study design would not be possible as we do not have one specific intervention to give to participants such as the giving of corticosteroids in patients with severe community acquired pneumonia [177] or the prophylactic administration of probiotics to children in an intensive care unit [178].

Qualitative study designs such as interviews or focus groups were also considered. Although there is the increased risk of recall bias with these methods due to the participants having dementia, past studies have shown that conducting focus groups with PWD are possible. Sutcliffe et al. [179] used focus groups (n=27) to explore PWD and their carers' experiences of dementia care and services and Strandenæs et al. [180] conducted individual interviews with 17 PWD who attended day care. Both of these methods may have been able to provide a detailed and more comprehensive picture of what potential risk factors may have contributed to the development of pneumonia in PWD but due to the qualitative study designs, any conclusions would not be able to be generalised to the larger population or provide information on which risk factors are more prevalent.

The final study design which was considered for a future study was a case-control study design. Case-control studies are designed to help determine if an exposure is associated with an outcome such as a specific disease. One such study using this design which wanted to determine whether statins and ACE inhibitors/angiotensin receptor blockers were associated with reduced risks of pneumonia. The study had 19,281 cases (patients who

were hospitalised for pneumonia) and 19,281 controls [181]. This study had a similar research question to our own which shows how the use of a case-controlled study design could be used to determine the association between a number of potential risk factors and pneumonia in PWD.

Case-controlled studies have a number of advantages [182]:

- They are comparatively quick, inexpensive and easy to conduct
- Particularly appropriate for:
    - Investigating outbreaks
    - Studying rare diseases or outcomes
- Due to their efficiency, they may be ideal for preliminary investigations of a suspected risk factor for a common condition – conclusions may be used to justify a more costly and time-consuming longitudinal study later
- Can study multiple exposures

Their disadvantages include:

- They cannot generate incidence data
- Are subject to bias
- Selection of controls can be difficult

A case-controlled study design was therefore chosen to be the most appropriate study design for a future study, as it would allow the association between a variety of potential risk factors and the development of people with dementia developing pneumonia to be determined. It would be quicker than other study designs to conduct yet would still utilise a large enough sample size for the results to be generalisable. Cases would be defined as participants diagnosed with pneumonia and controls would be those without pneumonia. A nested case-controlled design would ensure that all included participants had a diagnosis of dementia. Risk factors to be included from the previously conducted literature search during chapter 1 would be chosen based on their relevance to being incorporated into a community pharmacy tool (such as medicines, formulations, oral health, influenza vaccination) and their availability in study data sources.

Future case-control study setting

A setting was needed where patients would be identified with dementia and pneumonia. With dementia patients generally being over the age of 60 and being more vulnerable, they are more likely to require hospital treatment for their pneumonia [183]. A hospital setting (compared to a primary care setting) would therefore be the most sensible location for a future prospective case-controlled study.

The university is associated with a neighbouring teaching hospital where there are strong relationships between the academic and clinical staff. This hospital was chosen to be the ideal setting for a future case-controlled study.

3.2.2 Prospective cohort study rationale

Due to the researcher being a community pharmacist, the information contained within hospital-based potential data sources for a future case-control study were unknown. The researcher was therefore unsure what risk factors would have data available for collection and which sources would be the most useful.

It was also unknown to the researcher how many eligible patients were admitted to the local hospital and therefore how long a future case-control study may need to run for in order to gain a large enough sample size. Previously conducted case-controlled studies exploring risk factors for pneumonia range from an enrolled 104 case-controlled pairs during a prospective 12 month study [72] to 543 case-control pairs (1:4 ratio) in a retrospective study using 18 years of dispensing history data [71].

The researcher therefore needed to firstly conduct a small prospective cohort study to analyse ward admissions on a relevant ward at the local hospital to: (i) determine the potential length of time required to reach a sufficient sample size and (ii) determine which risk factors are documented in medical notes and could therefore be included in a future case-control study.

3.3 Aim

To test the feasibility of conducting a future case-control study at the local hospital which would aim to identify the risk factors related to pneumonia related hospitalisation in PWD.

Objectives

- Identify which risk factors are documented in the data sources
- Describe how each risk factor is documented in the data sources
- Identify which record sources would be required to enable effective data collection
- Calculate the frequency that the risk factors are documented in the data sources
- Estimate the potential study population size for a larger case-controlled study

3.4 Methodology

3.4.1 Study Design

This was a prospective cohort study (PCS)

3.4.2 Setting

This study was conducted exclusively on a care of the older person ward at the local hospital which specialises in older people's medicine, including dementia. This specific ward was chosen because it is the most likely ward for PWD to be staying and would therefore be the best place to collect data on PWD.

3.4.3 Study Participants

Recruitment

The researcher visited the ward once a week for a total of 5 weeks between 23.10.15 and 25.11.15. On each visit, the medical note trolleys were carefully searched for new patient names against a reference sheet (Appendix 7) which contained the names of all previously searched notes. Where medical notes could not be found in their usual storage location, every effort was made to locate them elsewhere on the ward.

Inclusion criteria

All patients admitted during the data collection period between 23.10.2015 and 25.11.2015 dates were included.

Exclusion criteria

Patients were excluded if their notes were unavailable during the data collection visits or if they were both admitted and discharged from the ward during the days between ward visits by the researcher.

3.4.4 Data Collection

Each patient on the ward had three different data sources searched for any of the risk factors (age, gender, stage of dementia, residency, dysphagia, smoking history, pneumonia, aspiration, influenza vaccination, comorbidities, oral health, and prescribed medicines information) documented on the checklist tool (Appendix 8). These risk factors were chosen following the literature search documented in chapter 1 and were factors deemed to have the potential to be targeted in a community pharmacy designed tool.

The three data sources searched consisted of:

- Hard copy medical notes which contained vast quantities of information from various sources and the written notes from healthcare professionals
- Blue observation notes which were kept by the patient's bedside and recorded observation information such as food and drink intake and blood glucose levels
- Electronic Prescribing and Medication Administration (EPMA) records which the researcher has gained access to prior to the PCS commencing. The EPMA records mostly contained information on the medicines administered to each patient.

Each data source was carefully examined for each patient on the ward and created a new line on the checklist (Appendix 8) with a unique reference number for each patient. When any mention of any of the risk factor variable or pneumonia were recorded, the researcher ticked the relevant box on the checklist and made further notes where appropriate (such as how it was recorded in the notes).

3.4.5 Pilot

The first week of data collection was used to calculate the baseline number of patients on the ward for consequently estimating the average number of patients admitted to the ward each week. This first week of data collection also provided an opportunity to pilot the checklist tool and to make the following amendments:

- The additional checklist item 'dementia diagnosis' was added to the checklist as it became clear that this was also not always recorded and that not every patient on the ward had dementia.

- The EPMA records ceased being searched as a data source as it transpired that they did not contain any additional information than what was recorded in the hard copy medical notes.

3.4.6 Sample Size

Due to one of the objectives of this PCS being to estimate the potential study population size for a larger case-controlled study, no sample size calculation was required.

3.4.7 Confidentiality

To ensure confidentiality, no names were documented on the checklist and each patient was provided with a unique reference number. The reference sheet (Appendix 7) which contained the patient names and reference numbers was kept on the researcher during the ward visits at all times and kept in a secured room on the hospital ward between visits and for 6 months following the end of the study before the reference sheet was destroyed.

Data analysis was performed using the anonymous checklists completed during data collection and so no members of the researcher's supervisory team had access to confidential information.

3.4.8 Ethical approval

Ethical approval was not required for this study due to not being classified as 'research' according to the Health Research Authority [184]. A letter of access (Appendix 9) was received from the hospital on 08/09/15 however as good practice and to ensure that the researcher could gain access to the appropriate ward with the use of a hospital issued NHS card.

3.5 Results

3.5.1 Risk factor variables documented in the patient medical notes

Table 26 outlines which medical record sources contained information regarding each risk factor. It is clearly seen that the medical notes contained almost all the information required whereas the blue notes only had information corresponding to oral health and dysphagia. The EPMA data (as discussed above in regard to the pilot week), only contained data on the medicines and smoking status.

Table 26. Presence of risk factor information from each data source

Variable	Medical notes	Blue Notes	EPMA*
Stage of dementia	✓	X	X
Age	✓	X	X
Gender	✓	X	X
Residency	✓	X	X
Dysphagia	✓	✓	X
Smoking History	✓	X	✓
Pneumonia	✓	X	X
Aspiration	✓	X	X
Medicines before admittance:			
Name	✓	X	✓
Form	✓	X	✓
Dose	✓	X	✓
Dissolve/half/crush	✓	X	X
Vaccine	X**	X	X
Co-morbidities	✓	x	X
Oral health	✓	✓	X
Dementia diagnosis	✓	X	X

**Electronic Prescribing and Medicines Administration system. ** Only one record was found within the medical notes*

3.5.2 Risk factor documentation and reliability

Table 27 summarises how commonly each risk factor was found in the data sources combined and how it tended to be documented. Demographic data and basic medicine information such as age, gender, medicine names and doses were commonly found in the data sources (i.e. virtually found in every case), whereas several of the potential risk factors and an actual pneumonia diagnosis were rarely found (i.e. only found in 5 or less cases). Those 'sometimes found' (such as medicine formulation) were seen in more than 5 cases but not found in each case.

Table 27. The reliability of risk factor documentation within medical notes and where is may be found

Variable	Commonly found	Sometimes found	Rarely found	How documented
Stage of dementia		✓		AMT* section in some notes. Not always completed.
Age	✓			Several times in various areas of the notes
Gender	✓			
Residency	✓			
Dysphagia			✓	Have to read notes thoroughly for details from a SALT** or dietitian. Perhaps some information in blue notes but none found of use.
Smoking History			✓	Status on EPMA*** and clinical notes rarely completed. Possibly only completed if ARE a smoker.
Pneumonia			✓	Definite diagnoses rarely documented. Often treat for symptoms without diagnoses often being known.
Aspiration			✓	Only saw a few cases where aspiration reported in notes.
Medicines before admittance: *Name* *Form* *Dose* *Dissolve/half/ crush*	 ✓ ✓	 ✓	 ✓	Name often found in admittance notes or at the back of the folder in past MAR# charts. When no further information provided by GP## or residence, form was often not documented. Rarely further comments in medical notes about form or using devices to aid adherence.
Vaccine			✓	Not documented in any parts of notes.
Co-morbidities	✓			Usually documented in the medical notes on admittance or at the back of the notes provided by GP##.
Oral health			✓	Blue observation notes included a section called 'body and oral hygiene' which was completed in regard to body hygiene more than oral hygiene. No other oral information is provided in notes except for very rare report of dentures on patient property forms.
Dementia Diagnosis		✓		There is a space on the admittance forms for dementia status but it was not always completed. Most patients with dementia had a blue sticker in their notes to represent dementia.

**Abbreviated Mental Test; **Speech and Language Therapist; ***Electronic Prescribing and Medicines Administration system; #Medicine Administration Record; ## General practitioner*

3.5.3 Number of patients with dementia

The mean number of new patients with dementia admitted to the ward between weeks 1 to 5 was 6.4. The numbers of new patients admitted each week are presented in Table 28.

Table 28. Number of patients with a diagnosis of dementia admitted to the ward per week

	Week number and date of data collection					
	0* 23.10.15 (n=34)	1 27.10.15 (n=8)	2 2.11.15 (n=13)	3 11.11.15 (n=14)	4 18.11.15 (n=10)	5 25.11.15 (n=15)
Dementia, n (%)	16**(47)	2 (25)	7 (54)	9 (64)	6 (60)	8 (53)

**Baseline figures discarded from mean calculations; **First 6 cases did not have dementia status documented so were recorded as 'na'.*

3.5.4 Proportion of patients with dementia and a swallowing difficulty and/or pneumonia

Discounting baseline figures, the mean number of patients admitted with dementia to the ward with a swallowing difficulty between weeks 1 and 5 was 1.6 patients per week.

The mean number of patients admitted with dementia and pneumonia during the same timespan was 1.4 patients per week.

The weekly figures are presented below in Table 29.

Table 29. Number of patients with a diagnosis of dementia and pneumonia and/ or a swallowing difficulty

	Week					
	0* (n=34)	1 (n=8)	2 (n=13)	3 (n=14)	4 (n=10)	5 (n=15)
Dementia and swallowing difficulty, n (%)	2 (5.8)	0 (0.0)	2 (15.4)	3 (21.4)	0 (0)	3 (20.0)
Dementia and pneumonia, n (%)	2 (5.8)	1 (12.5)	1 (7.7)	3 (21.4)	2 (20.0)	0 (0.0)

**Baseline figures discounted from mean calculations*

3.6 Discussion

Written medical notes were the most informative data source but many of the risk factors or a clear pneumonia diagnosis were rarely documented in any data sources. The risk factors which were found to be commonly documented were often present in a variety of ways and in differing areas of the medical notes.

The mean number of patients admitted to the ward with dementia each week was 12 with a mean of these patients having pneumonia being just 1.4.

A strength of this study was that it was a feasibility study to determine the viability of a future case-control study at this site, allowing the researcher to explore quantitative and qualitative methods of data collection. The study also allowed a variety of potential risk factors to be explored and to assess whether the data sources would provide enough information for a future case-control study.

Researcher unfamiliarity with hospital systems, written and observation notes may have led to misinterpreted or missing data.

The timing of this study was in winter at a time when admissions for pneumonia and other complications in the elderly are higher. This means that the number of patients being admitted is likely to be at a higher level compared to other times of the year and that the average mean of patients per week is actually much lower that was reported in this chapter.

This time of year also leads to the ward being very busy which led to times when certain medical notes were unavailable or misplaced at the time of need. There is therefore the potential that not every patient on the ward during this time was documented. This is enhanced by the fact that the visits were weekly which resulted in patients that were admitted for less than a week potentially not being documented.

The result that the written medical notes were the most informative source of data could potentially be a barrier to the design of a future case-control study as it is very time consuming. The handwritten notes were often difficult to read and contained a variety of unfamiliar abbreviations. Poor handwriting and the illegibility of handwritten medical notes has been documented in other studies. Rodriguez-Vera et al. reported 15% of their medical records sample (n=117) had defects of legibility making the record unclear [185] and Baigrie et al. [186] noted how approximately 70% of operation notes (n=264) written by consultant in two general hospitals were illegible or the procedure could not be

understood from the description given. These difficulties at times made the interpretation of the notes difficult and at times subjective. Ideally, a future case-control study would use a quicker and more reliable method off accessing the data such as comprehensive electronic records which have fully replaced written notes. This PCS found however that the electronic records at the local hospital are not used to their full potential as of yet and do not have the ability to document all of the information currently recorded in written notes.

In addition to the handwritten notes sometimes being illegible or heavily abbreviated, a large number of the chosen risk factors did not seem to be documented unless they were present. For instance, smoking status was often not present unless they were a smoker. Some risk factors were generally not documented at all (such as vaccinations) and so other sources for this data would have to be considered during study design.

Limitations with using manual chart review as the primary data source has also been documented in other studies. Tinoco et al. [187] retrospectively analysed inpatient adverse drug events and hospital-associated infections using computerised surveillance systems (CSS) and manual chart reviews (MCS). The CSS detected a much greater proportion of adverse drug events compared to the MCS (92% versus 34%) which reinforces that relying on manual chart review as a primary data source in a case-controlled study would not be ideal as it would most likely not pick up all possible participants. However, the exclusive use of other data sources should be carefully considered too, as some studies, such as Preen et al. [188] have reported large discrepancies between administrative, primary and secondary care sources of patient information.

The documentation of risk factors was further made complicated since those which were recorded, tended to be recorded in a variety of ways and in a number of places within the notes. This means that for each participant, every aspect of the notes would need to be reviewed which would add to the time consuming and inefficient nature of manually reviewing medical notes for a future case-control study.

Notes highlighted that diagnoses (such as dementia, or pneumonia) were rarely reported. Pneumonia was often hinted at by the recording of other information such as chest sepsis or chest infection and dementia was sometimes either assessed in the form of an abbreviated mental test (AMT) or written within the main section of the notes. If this was to be conducted on a larger scale as part of a future case-controlled study, it would be difficult to define what would be classed as a dementia or pneumonia diagnosis or whether

the patient has dysphagia. The subjectivity of the researcher when interpreting the notes could lead to bias in the results such as an over-estimation in the numbers of patients with pneumonia (as some may not have pneumonia but some other respiratory infection). Again, this reinforces the message that using medical notes as the key data source to extract this type of information is not advisable for a future case-controlled study.

Another issue which these results brought to light was that many of the patients in this PCS who were classed on the checklist as having a diagnosis of dementia were not formally assessed or diagnosed prior to admission. Instead, they were diagnosed within the notes during their hospital stay. This was a similar scenario for dysphagia also. A future case-control study would have to consider carefully which patients would be defined as having dementia / pneumonia/ dysphagia as this would greatly alter estimated sample sizes.

The mean number of patients being admitted to the ward was a reasonable number for the size of the ward but as discussed in the limitations, this is likely to fluctuate throughout the year and this must be taken into consideration when designing the time and length of a future case-control study. To overcome this, many prospective, hospital based case-controlled studies run for lengthy periods such as 2 [189] to 5 years [190].

There were very few patients admitted to the ward with dementia and pneumonia or a swallowing difficulty. In order to reach a similar sample size to Vergis et al [72] of 104 pairs (which used similar methodology to how a future case-control study would be conducted at the local hospital) the study would need to run for over 2 years and this is without taking dementia severity/ consent/ admission fluctuations/ unexpected complications into account. The length of time would therefore be nearer 3 years to ensure sufficient numbers and this length of time is not feasible during the time of the PhD.

3.7 Chapter conclusion and development of logic model

Following this small PCS, it was concluded that conducting a future case-controlled study at the hospital with medical notes as the main data source would not be a viable option. It would be impossible to recruit the large sample size required within a reasonable timeframe and the notes were not sufficiently reliable for use for data collection.

Therefore, a different data source is required to meet the research aims.

Due to this being a feasibility study to guide the development of a future case-controlled study, no new data regarding the logic model (Figure 9) was gained.

3.8 Next Steps

After learning that a case-control study within secondary care would not be feasible, the next steps were to consider possible options for a study within primary care and using an alternative data source which doesn't involve manually reviewing medical notes. It was at this time that we became aware of a large primary care electronic database which contains detailed clinical information of a large proportion of the UK population.

The next chapter, Chapter 4 introduces this database in more detail and guides the reader through the case-control study, which we were able to then conduct.

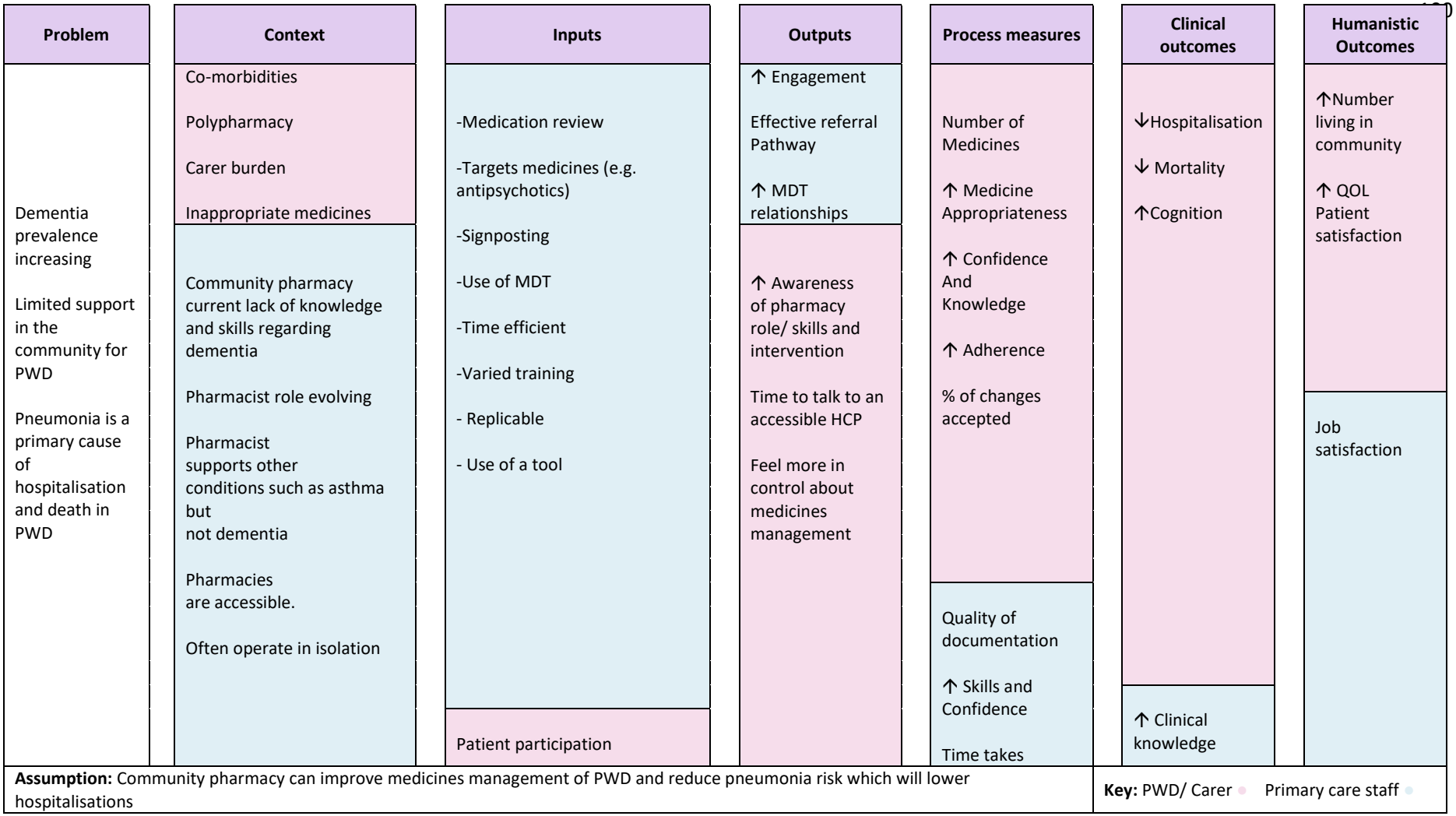

Figure 9. Logic model after feasibility study

Chapter 3. Analysis of ward admissions

Chapter 4.

Nested case-controlled study using CPRD data

4.1 Chapter outline

After concluding in Chapter 3 that the initially proposed case-control study at the local hospital would not be a viable option, this chapter introduces the reader to the primary care based digital database, CPRD and describes the case-control study which was conducting using this alternative data source.

4.2 Introduction

The Clinical Practice Research Datalink (CPRD) is a governmental, not-for-profit research service which is jointly funded by the National Institute for Health Research (NIHR) and the MHRA. CPRD provides anonymised primary care records for public health research from GP practices across the UK which includes over 20 million patients, of which 5 million are currently registered and active [191]. The use of this database meant that the study would be comparatively quick and financially favourable because there would be no recruitment of patients or the collection of data over a lengthy period. Additionally, due to this database including a very large proportion of the UK population, the study would be able to use a large sample size which should mean that the study will have more power and be able to detect any associations more accurately.

Patients experiencing dysphagia can find swallowing their prescribed medicines difficult. Residents in one study (previously reported in section 1.6.2) who were unable to swallow their oral medication were associated with being eight times more likely to develop pneumonia (OR: 8.3, 95% CI 1.4 to 50.3, p=0.02) [49]. This study did not specify why they were unable to swallow their medicines (for example, did they have dysphagia or were the tablets too big for them to swallow) or what oral formulations were included in this analysis. The latter is an important aspect to be considered because there are various oral formulations (such as tablets, liquids, orodispersible tablets and buccal tablets) and the outcomes for each could be different. Additionally, the small sample size and broad 95% CI calculated means that the true association between these two variables (dysphagia and pneumonia) is unknown.

There is a dearth of research which explores specific formulations and their associations with pneumonia and in particular in PWD. This study will therefore firstly determine if a true association between dysphagia and pneumonia exists in a dementia cohort and also whether the association is dependent on the type of formulations prescribed.

Although section 1.6.2 identified a range of other potential risk factors for developing pneumonia, many of these were not conducted in a dementia specific cohort. This study will therefore also build on the previously identified evidence in section 1.6.2 and determine if any of the previously identified potential risk factors are associated with developing pneumonia in PWD. Risk factors from section 1.6.2 were therefore included in this study if:

- They were routinely documented in primary care would be available within the database,

  and either:
- Further affirmation of their association with pneumonia would be beneficial in general, or
- They were factors which could be targeted as part of the intervention and further information on their associations with pneumonia would be useful.

Table 30 reviews the risk factors identified in section 1.6.2 and summarises the rationale for why the risk factors included in this case-control study were chosen:

Table 30. Summary of risk factors to include in study

Identified possible risk Factor	**Included because:**		**Not included**
	Could be targeted in a community pharmacy intervention	Beneficial to include to acquire further data on association with pneumonia in PWD	
Dysphagia	✓	✓	
Tube feeding			✓
Medicine formulation	✓	✓	
Antipsychotics	✓	✓	
PPI			✓*
Residence			✓
Gender		✓	
Oral Health			✓
Smoking	✓	✓	
Co-morbidities (Influenza, COPD, CVD, DM, stroke, head, neck cancer**)	✓	✓	
ACE inhibitors	✓	✓	
Pneumococcal vaccine	✓		
Influenza vaccine	✓		

**Decided not to include in order to concentrate on the antipsychotics and ACE inhibitors; **Included as would be a logical confounder*

4.3 Aims and Objectives

The overall aim is to determine whether dysphagia is associated with incident pneumonia among patients with dementia and whether the formulation of common medication can moderate any effect.

Primary Objectives

- To calculate the proportions of cases and controls with a diagnosis of dysphagia
- To calculate the proportions of cases and controls prescribed different formulations of: paracetamol; risperidone; fluoxetine; furosemide and donepezil
- To estimate the association between dysphagia and pneumonia in patients with dementia
- To determine if particular formulations of medicines moderate any observed association between dysphagia and first incident pneumonia after being diagnosed with dementia

Secondary Objectives

- To estimate the association between incident pneumonia and a range of covariates that are hypothesised to potentially confound the link between dysphagia and pneumonia

4.4 Method

Initially the data was prepared for use by a statistician who had experience in both STATA and CPRD. The preparation phase consisted of accessing the data from the CPRD database as the CPRD key holder, generating the cases and controls using specific CPRD software and pre-prepared (by the researcher) lists of READ codes to put inclusion and exclusion criteria in place and to generate the required variables.

4.4.1 Study Design

A nested case-control study design was chosen (where all those included had a diagnosis of dementia) in order to retrospectively estimate the association of pneumonia with a broad range of exposures.

A conventional case-control study simply involves cases (those with the disease of interest) and controls (a group of individuals without the disease of interest) and allows the comparison of these separate groups for variables of interest. A **nested** case control study

involves an additional layer of screening as all participants (cases and controls) belong to a defined cohort with a specified number of controls being selected from the cohort who have not developed the disease (in this case dementia) by the time of the disease occurrence in the case (known as the index date) [192].

The research question is regarding only PWD and therefore, nesting the study within a population of those with dementia is advantageous. Additionally, this study design requires the matching of controls to cases (usually in a ratio) using variables such as age, gender or area which helps reduce selection bias. This design does therefore require a large dataset (which CPRD can provide) and as with case-controlled studies, can only determine possible associations of variables and outcomes and cannot provide results for true causality.

4.4.2 Sample Size

A feasibility analysis of CPRD conducted by the statistician suggested that there were 89612 cases of incident dementia with at least 3-month follow-up post diagnosis and 6 months of up to standard (UTS) data prior to diagnosis (May version of CPRD GOLD). UTS data is data recorded by the practice after the UTS date, which is a practice-based quality metric based on the continuity of recording and the number of recorded deaths. The UTS date for each practice is the date at which the practice has met the minimum quality criteria.

A sample size calculation was also conducted by the statistician (using Stata version 14.1 power mcc routine) which found that with assuming 4:1 control to case matching, using a threshold of $p<0.01$ for statistical significance on a two-sided test, the estimated smallest size of association that is detectable with 80% power, given binary risk factors of varying prevalence in the control group are as follows:

- For a potential risk factor with a prevalence of 50% among controls, we will be able to detect an OR of 1.10
- For a potential risk factor with a prevalence of 10% among controls, we will be able to detect an OR of 1.16
- For a potential risk factor with a prevalence of 2% among controls, we will be able to detect an OR of 1.35

4.4.3 Data Linkage

Linkage to the Index of Multiple Deprivation (IMD) was performed in order for IMD to be a covariate for adjustment. IMD scores based on practice postcodes were used in order to

retain maximum sample size and provided information on the patient socioeconomic status (SES) of the patients.

4.4.4 Study Population

Case AND control inclusion criteria

All included patients had a new diagnosis of dementia by any of the READ codes selected by the researcher and confirmed by an academic with a medical background. There had to be at least 180 days of up to standard (UTS) data available prior to dementia diagnosis to ensure that only new cases of dementia were captured. The period of patient follow-up started from the latest from either the current patient registration date or the surgery UTS date. The period of follow-up ended from the earliest of either at the last collection date, the transfer out date (such as to another surgery) or death date. There were no age restrictions.

Case AND control exclusion criteria

Dementia patients with a pneumonia diagnosis within 90 days after the dementia diagnosis were excluded. This was to ensure that the first recorded pneumonia incident was not due to a complication which may have occurred prior to the dementia diagnosis.

Patients with any codes which could suggest an informal dementia diagnosis prior to a formally recorded dementia diagnosis at a later date were excluded to ensure that all included patients definitely had dementia.

Patients who had 2 different formulations of the same medicine from either: paracetamol; risperidone; fluoxetine; furosemide or donepezil within 30 days prior to index date were also excluded which ensured that any results observed could be associated with particular medicine formulations.

Any patients that had missing gender or IMD quintiles were also excluded from the analysis.

Case ONLY additional inclusion criteria

Patients who received a diagnosis of pneumonia as documented by any of the READ codes selected by the researcher and confirmed by the medical academic mentioned earlier were included and the first pneumonia diagnosis post dementia diagnosis defines the index date.

4.4.5 Selection of controls

Up to 4 controls were identified per case. They were matched on index date, dementia diagnosis year, region and birth year (±3 years). Controls were selected from the pool of patients with dementia who did not have a diagnosis of pneumonia between dementia diagnosis and their matched case index date. To ensure that the study had the largest sample size possible and utilised all possible patients, incidence density sampling was used which meant that cases were eligible to be controls for other cases. A summary of the inclusion and exclusion criteria can be found in Figure 10.

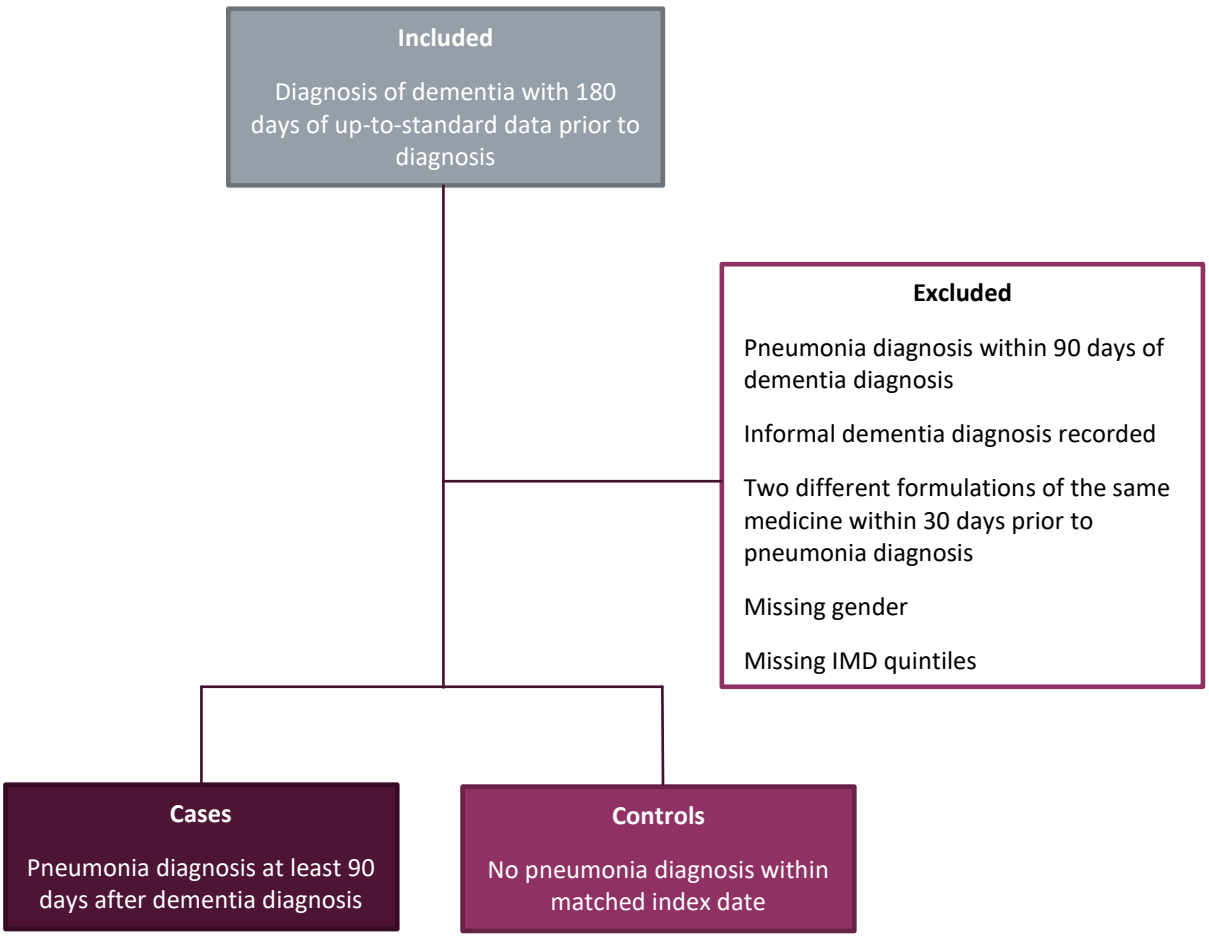

Figure 10. Visual summary of inclusion and exclusion criteria

4.4.6 Primary Exposures

Dysphagia

Dysphagia was recorded as being present by either:

- Listed in the notes by use of any READ codes selected by the researcher and confirmed by the medical academic
- Presence of approved product codes for feed thickeners / pre-thickened drinks which suggest a swallowing problem. Any product needed to have been prescribed at least twice in 6 months prior to index date to ensure it was just needed for a short time or was just a trial

Medicine Formulation

Due to it not being feasible to assess every medicine and formulation that has been prescribed, specific medicines were chosen which are commonly prescribed in both a solid and an alternative formulation and common in patients with dementia. Table 31 summarises the medicines chosen and rationale. Any presence of any of the selected medicines within 30 days of the index date were recorded.

Table 31. Selected medicines for formulation exploration

Medicine	Rationale	Formulations
Paracetamol	Common for pain relief	Tablet, effervescent, soluble tablet, orodispersible tablet, capsule, oral suspension, oral solution, solution for infusion, suppository, powder for suspension
Risperidone	Licensed in Alzheimer's Disease for short-term treatment of persistent aggression	Tablet, Orodispersible tablet, oral solution, powder and solvent for suspension
Fluoxetine	Patients with dementia may need treatment for depression	Dispersible tablet, capsule, oral solution
Furosemide	Elderly people often prescribed this for treatment for oedema or hypertension	Tablet, oral solution, solution for injection
Donepezil	Prescribed to reduce the symptoms of dementia in Alzheimer's Disease	Tablet, orodispersible tablet, oral solution

4.4.7 Secondary Exposures

The following secondary exposures were recorded for further analysis:

- Gender
- The prescription of ACE inhibitors and first and second antipsychotics
- Smoking status
- Documentation of a diagnosis of influenza within 1 year prior to index date
- Presence of: COPD, heart disease, diabetes, stroke or head or neck cancer
- Presence of influenza vaccination in the 1 to 3 years prior to index date
- Presence of pneumococcal vaccination

4.4.8 Outcome

After a washout period of 3 months since dementia diagnosis, the first incidence of pneumonia was recorded.

4.4.9 Covariates

As previously mentioned, the additional variable of IMD scores were recorded as it could have been a potential confounder.

4.4.10 Data/ Statistical Analysis

The distributions and proportions of all exposures and the covariate were compared between pneumonia and non-pneumonia groups. Conditional logistic regression (CLR) followed in steps 1 and 2 where Odd Ratios (ORs) with 95% confidence intervals were calculated. P-values were classed as significant where $p \leq 0.01$.

1. CLR with pneumonia as the outcome and dysphagia only (**formulations not included in this analysis**) plus secondary exposures and covariates as predictors. This determined whether there was an association between dysphagia and pneumonia in a dementia specific cohort, and allowed secondary exposures to be explored.
2. CLR as step 1 but with the addition of medicine formulations as an exposure, to determine any interactions between each medication formulation and dysphagia. The size of the interaction effect for each formulation of each medication with dysphagia, compared to no formulation present indicated whether the formulation altered the association between pneumonia and dysphagia or the secondary exposures and covariates.

3. A sensitivity analysis was conducted to test the association of medication formulation restricted only to those with dysphagia.

Data analysis was conducted using Stata version 14, 64-bit SE.

4.4.11 Confounding

All variables were adjusted for during the CLR analysis in order to minimise any confounding.

4.4.12 Missing data

Missing data for 'smoking status' was coded within the data as 'missing/unknown'. Individuals with missing smoking history were assigned into a 'missing' category and included in the analysis.

Missing vaccination history was treated as 'no vaccination' and all other variables didn't have the potential for missing data as they were in a binary format as either 'present' / 'not present'.

4.5 Results

4.5.1 Study Approval

Initial feedback from the Independent Scientific Advisory Committee (ISAC) was gained on 24/10/16 (Appendix 10) and subsequent approval of protocol 16_210R received on 13/01/17 (Appendix 11).

4.5.2 Total cases and controls

The final dataset incorporated of 28,671 controls (no diagnosis of pneumonia) and 7,259 cases (diagnosis of pneumonia).

4.5.3 Demographics

The majority of participants were female across the full dataset but there were almost double the proportion of men in the case group (29.9%) compared to the control group (42.1%). The mean age was 84 years, England was the most common country (75%) and there was a slight trend for the proportion of participants to increase as the IMD score increased. Table 32 presents these results in more detail with further information in Appendix 12.

Table 32. Participant demographics

	Control (n= 28,671)	**Case (n= 7,259)**
Male, n (%)	8,571 (29.9)	3,058 (42.1)
Age, mean (SD)	84.4 (7.2)	84.4 (7.7)
Country, n (%)		
England	21,519 (75.1)	5,449 (75.1)
Northern Ireland	1,631 (5.7)	419 (5.8)
Scotland	3,060 (10.7)	768 (10.6)
Wales	2,461 (8.6)	623 (8.6)
IMD score*, n (%)		
1	2,674 (9.3)	644 (8.9)
2	2,547 (8.9)	791 (10.9)
3	2,761 (9.6)	62 (8.6)
4	2,076 (7.2)	473 (6.5)
5	2,584 (9.0)	575 (7.9)
6	2,652 (9.3)	558 (7.7)
7	3,264 (11.4)	861 (11.9)
8	3,129 (10.9)	814 (11.2)
9	3,569 (12.45)	1,065 (14.7)
10	3,415 (11.9)	854 (11.8)

**Index of multiple deprivation (the higher the IMD score, the more deprived)*

4.5.4 Co-morbidities

In both groups, cardiovascular disease was the most common co-morbidity and head/neck cancer was the least common (see Table 33). Cases however had almost double (10.9%) the proportion of COPD cases compared to the controls (5.5%) and over 4 times (9.4%) the proportion of dysphagia cases compared to controls (2.8%).

Table 33. Frequency data for co-morbidity variables

Co-morbidity	**Control (n= 28,671)**	**Case (n= 7,259)**
Stroke, n (%)	2,075 (7.2)	2,893 (8.05)
Chronic Obstructive Pulmonary Disease, n (%)	1,574 (5.5)	791 (10.9)
Cardiovascular disease, n (%)	5,781 (20.2)	1,750 (24.1)
Diabetes, n (%)	3,492 (12.2)	1,009 (13.9)
Head/neck cancer, n (%)	32 (0.1)	8 (0.1)
Dysphagia, n (%)	810 (2.8)	683 (9.4)

4.5.5 Vaccinations, previous influenza diagnosis and smoking status

The majority of participants in both groups has received their influenza vaccination within 1 year of the index date and their pneumococcal vaccination at some point in time (see Table 34). Cases had over 20 times more influenza diagnoses (2.1%) compared to controls (0.1%) but the majority of both groups were non-smokers.

Table 34. Vaccination, influenza diagnosis and smoking status

Variable	Control (n= 28,671)	Case (n= 7,259)
Influenza vaccination, n (%)		
No vaccination recorded	8,847 (30.8)	1,952 (26.9)
Within 1 year of index date	14,066 (49.1)	3,653 (50.3)
Within 3 years of index date	5,758 (20.1)	1,654 (22.8)
Influenza vaccination, n (%)		
Not in 1 year prior index date	14,605 (50.9)	3,606 (49.7)
Within 1 year prior index date	14,066 (49.1)	3,653 (50.3)
Pneumococcal vaccination, n (%)		
No vaccination recorded	11,640 (40.6)	2,917 (40.2)
Within 1 year of index date	981 (3.4)	204 (2.8)
Vaccination recorded at some time	15,606 (54.4)	3,994 (55.0)
Under 65 at index date	444 (1.6)	144 (2.0)
Pneumococcal vaccination, n (%)		
No vaccine ever	12,084 (42.2)	3,061 (42.2)
Had a vaccine ever	16,587 (57.9)	4,198 (57.8)
Influenza Diagnosis*, n (%)	38 (0.1)	155 (2.1)
Smoking Status, n (%)		
Non-smoker	16,567 (57.8)	3,701 (50.9)
Ex-smoker	6,713 (23.4)	2,012 (27.7)
Smoker	2,016 (7.0)	616 (8.5)
Missing	3,375 (11.8)	930 (12.8)

**Diagnosis within 1 year of index date and including index date (see appendix 1 for further information)*

4.5.6 Medicines

Table 35 shows the proportions of cases and controls prescribed ACE inhibitors and antipsychotics. A higher proportion of controls were prescribed ACE inhibitors whereas a slightly higher proportion of cases were prescribed both first and second generation antipsychotics.

Table 35. Proportions of case and controls prescribed certain medicine groups

Medicine group	Control (n= 28,671)	Case (n= 7,259)
Angiotensin Converting Enzyme inhibitor, n (%)	3,545 (12.4)	666 (9.2)
Antipsychotic (1st generation), n (%)	1,396 (4.9)	537 (7.4)
Antipsychotic (2nd generation), n (%)	1,419 (5.0)	383 (5.3)

4.5.7 Medicine formulations

Table 36 summarises the frequencies for the different medicine formulations for cases and controls. Please see Appendix 12 for the individual results for the medicines tested (donepezil, fluoxetine, furosemide, paracetamol and risperidone).

The majority of both cases and controls did not receive any of the recorded medicines and therefore formulations. The most common formulation prescribed was oral solids for both controls (34%) and cases (29%) with non-oral being the least prescribed.

Table 36. Frequencies of medicine formulations for cases and controls

	Control (n= 28,671)	**Case (n= 7,259)**
Had no formulations recorded, n (%)	18,107 (63.2)	4,647 (64.0)
Non-oral, n (%)	0 (0.0)	26 (0.4)
Oral Solid, n (%)	9,742 (34.0)	2,103 (29.0)
Oral Liquid, n (%)	671 (2.3)	383 (5.3)
Oral solid + oral liquid, n (%)	150 (0.5)	94 (1.3)
Non-oral + oral solid, n (%)	0 (0.0)	4 (0.1)
Non-oral + oral liquid, n (%)	1 (0.0)	2 (0.0)

4.5.8 Unadjusted Odds Ratios

The unadjusted odds ratios (ORs) for each variable are reported below.

Co-variables

Table 37 summarises the unadjusted ORs for each co-variable. According to these results, females are associated with being half as likely to develop pneumonia, unlike smokers and ex-smokers who are both associated with an increased risk. Having dysphagia was associated with increasing the likelihood of developing pneumonia by more than 3.5 times and having COPD by double. A diagnosis of stroke was also associated with an increased the risk of developing pneumonia whereas head/neck cancer and diabetes did not show an association to pneumonia.

ACE inhibitors seemed to be associated with reducing the risk of developing pneumonia (0.72) whereas first generation antipsychotics were associated with increasing the risk of pneumonia by half (1.59). Having an influenza diagnosis including the index date was associated with increasing the likelihood of developing pneumonia by over 17 times. However, this high OR is based on small numbers being detected in both groups (hence the relatively large standard error of 3.35 and wide confidence interval (12.16 to 25.58) which may be due to a lack of accurately identifying or recording influenza (which may quickly develop into pneumonia) either in primary or secondary care.

Influenza vaccinations were also associated with an increased risk which seems counterintuitive but may be indicative of the types of people who receive a vaccination. Influenza vaccines are targeted at and free on the NHS for people such as those with

respiratory diseases (such as COPD and asthma), diabetes and chronic heart disease. All of which have also been shown to have an association with a higher risk of developing pneumonia within this study.

The pneumococcal vaccination had a minimal association to pneumonia when taken within the year before index date (0.83, CI: 0.70 – 0.98).

Table 37. Unadjusted odds ratios for each variable

Variable	Unadjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.57	0.54 – 0.60	< 0.001	0.02
Smoking Status:				
Non-smoker	1			
Ex-smoker	1.38	1.29 – 1.46	< 0.001	0.04
Smoker	1.40	1.26 – 1.54	< 0.001	0.07
Missing	1.19	1.08 – 1.31	< 0.001	0.06
Dysphagia:				
No	1			
Yes	3.57	3.20 – 3.98	< 0.001	0.20
COPD*:				
No	1			
Yes	2.16	1.98 – 2.37	< 0.001	0.10
Stroke:				
No	1			
Yes	1.64	1.51 – 1.79	< 0.001	0.07
Head/neck cancer:				
No	1			
Yes	1.02	0.47 – 2.23	0.952	0.41
Diabetes:				
No	1			
Yes	1.19	1.10 – 1.28	< 0.001	0.05
Cardiovascular disease:				
No	1			
Yes	1.27	1.20 – 1.35	< 0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.72	0.66 – 0.78	< 0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.59	1.43 – 1.77	< 0.001	0.09
Antipsychotic (2nd) **:				
No	1			
Yes	1.08	0.96 – 1.22	0.191	0.07
Influenza diagnosis#:				
No	1			
Yes	17.64	12.16 – 25.58	< 0.001	3.35
Influenza vaccination:				
Never	1			
Within 1 year	1.29	1.19 – 1.38	< 0.001	0.05
Within 3 years	1.47	1.35 – 1.60	< 0.001	0.07
Pneumococcal vaccination:				
Never	1			
Within 1 year	0.83	0.70 - 0.98	0.027	0.07
Had one at some point	1.07	0.99 – 1.15	0.070	0.04
Under 65 at index	1.98	0.97 – 4.06	0.061	0.73
Pneumococcal vaccination:				
No vaccination ever	1			
Had vaccination sometime	1.04	0.97 – 1.11	0.266	0.04

**Chronic Obstructive Pulmonary Disease; **1st or 2nd generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

Formulations

Table 38 summarises the unadjusted odds ratios for each formulation. This data suggests that prescribed solids only were associated with being slightly less likely to contract pneumonia whereas those prescribed only liquids were associated with being more than twice as likely to contract pneumonia. Interestingly, those prescribed a mixture of oral solids and liquids were at a slightly higher risk (2.48) of obtaining pneumonia compared to those prescribed only a solid (0.83) or a liquid (2.37).

The large OR calculated regarding those prescribed a non-oral formulation is due to the very small numbers who had this documented (0.4% of cases and 0% of controls). This is relayed in the very large standard error and wide confidence interval seen and suggests that no true conclusion can be made regarding non-oral formulations and their associations with developing pneumonia.

Table 38. Unadjusted odds ratios for medicine formulations

Formulation	Unadjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Non-Oral				
No	1			
Yes	124.05	16.95 – 907.96	<0.001	125.99
Oral Solid				
No	1			
Yes	0.83	0.78 – 0.88	<0.001	0.02
Oral Liquid				
No	1			
Yes	2.37	2.11 – 2.68	<0.001	0.14
Oral Solid + Oral Liquid				
No	1			
Yes	2.48	1.91 – 3.22	<0.001	0.33

4.5.9 Adjusted Odds Ratios

Adjusted odds ratios using various models are reported below.

Model 1: All co-variables *excluding* medicine formulations

Model 1 (Table 39) includes all possible co-variables but excludes the medicine formulations.

The ORs for each variable are not seen to change greatly compared to the unadjusted ORs.

Table 39. Adjusted odds ratios for model 1 which excludes medicine formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.60	0.57 – 0.64	< 0.001	0.02
Smoking Status:				
Non-smoker	1			
Ex-smoker	1.13	1.06 – 1.21	< 0.001	0.40
Smoker	1.25	1.11 – 1.37	< 0.001	0.07
Missing	1.21	1.09 – 1.34	< 0.001	0.06
Dysphagia:				
No	1			
Yes	3.46	3.09 – 3.87	< 0.001	0.20
COPD*:				
No	1			
Yes	1.97	1.79 – 2.18	< 0.001	0.10
Stroke:				
No	1			
Yes	1.50	1.37 – 1.64	< 0.001	0.07
Head/neck cancer:				
No	1			
Yes	0.78	0.34 – 1.80	0.563	0.33
Diabetes:				
No	1			
Yes	1.15	1.06 – 1.24	0.001	0.05
Cardiovascular disease:				
No	1			
Yes	1.19	1.12 – 1.27	< 0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.68	0.62 – 0.74	< 0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.56	1.40 – 1.74	< 0.001	0.09
Antipsychotic (2nd) **:				
No	1			
Yes	1.11	0.98 – 1.25	0.104	0.07
Influenza diagnosis#:				
No	1			
Yes	16.84	11.51 – 24.64	< 0.001	3.27
Influenza vaccination:				
Never	1			
Within 1 year	1.24	1.14 – 1.34	< 0.001	0.05
Within 3 years	1.43	1.31 – 1.57	< 0.001	0.07
Pneumococcal vaccination:				
Never	1			
Within 1 year	0.80	0.67 – 0.95	0.012	0.07
Had one at some point	0.93	0.86 – 1.00	0.050	0.04
Under 65 at index	1.84	0.86 – 3.95	0.117	0.72

**Chronic Obstructive Pulmonary Disease; **1st or 2nd generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

Model 2: All co-variables *including* **medicine formulations**

Model 2 (Table 40 and 41) includes all of the variables from model 1 but also includes the different medicine formulations in order to see what effect these have on the other co-variables. The ORs do not differ greatly from those seen in model 1 and the ORs relating to liquid formulations has only decreased slightly from the unadjusted figure of 2.37 to the adjusted figure of 2.02.

Table 40. Model 2 showing all co-variables and medicine formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.60	0.56 – 0.63	<0.001	0.02
Smoking Status:				
Non-smoker	1			
Ex-smoker	1.14	1.07 – 1.22	<0.001	0.04
Smoker	1.25	1.12 – 1.39	<0.001	0.07
Missing	1.20	1.09 – 1.33	<0.001	0.06
Dysphagia:				
No	1			
Yes	3.20	2.85 – 3.58	<0.001	0.19
COPD*:				
No	1			
Yes	2.01	1.82 – 2.21	<0.001	0.10
Stroke:				
No	1			
Yes	1.49	1.36 – 1.63	<0.001	0.07
Head/neck cancer:				
No	1			
Yes	0.79	0.34 – 1.82	0.579	0.34
Diabetes:				
No	1			
Yes	1.15	1.06 – 1.25	0.001	0.05
Cardiovascular disease:				
No	1			
Yes	1.20	1.13 – 1.28	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.69	0.63 – 0.76	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.53	1.37 – 1.70	<0.001	0.09

**Chronic Obstructive Pulmonary Disease; **1st or 2nd generation class of antipsychotic;*

Table 41. Model 2 showing all co-variables and medicine formulations - continued

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Antipsychotic (2nd) *:				
No	1			
Yes	1.09	0.97 – 1.24	0.156	0.07
Influenza diagnosis*:				
No	1			
Yes	17.20	11.74 – 25.21	<0.001	3.35
Influenza vaccination:				
Never	1			
Within 1 year	1.23	1.14 – 1.34	<0.001	0.05
Within 3 years	1.42	1.30 – 1.56	<0.001	0.07
Pneumococcal vaccination:				
Never	1			
Within 1 year	0.80	0.68 – 0.96	0.013	0.07
Had one at some point	0.93	0.86 – 1.01	0.083	0.04
Under 65 at index	1.78	0.83 – 3.82	0.136	0.69
Any formulations prescribed:				
Yes	1			
No	0.90	0.67 – 1.22	0.500	0.14
Oral formulation prescribed:				
No	1			
Yes	0.81	0.60 – 1.08	0.152	0.12
Liquid formulation prescribed:				
No	1			
Yes	2.02	1.54 – 2.66	<0.001	0.28

**1st or 2nd generation class of antipsychotic; ** Diagnosis within 1 year of index date and including index date*

4.5.10 Correlations

Due to the nature of the data (all nominal), accurately looking for correlations between the data was not possible. However, Spearmans rank was used to provide an overview of the data. The results (Appendix 13), as expected, did not show any significant correlations. Consequently, a more pragmatic approach to refining the model was taken.

Although there was an argument to keep all variables and potential confounders in the model as they all had rationale for potentially affecting the likelihood of developing pneumonia and removing any from the model may provide a less clear picture, it was decided to remove the variables which had similar proportions in both the case and control groups as logic dictates that these variables would therefore not be associated with a change in risk of developing pneumonia. Additionally, some variables (such as diabetes) were removed as it is known that there is a correlation between diabetes, CVD, and stroke [193]. For instance, in patients with type 2 diabetes, one study reported patients who experienced hypoglycaemia and had no history of CVD, had a hazard ratio of 1.49 (95% CI: 1.23 to 1.82) for a CV event [194]. Due to these risk factors already being correlated with

each other, there is no need for all of them to be in the final model (as if a patient was to have diabetes, they are also associated with being more likely to have CVD) and so therefore only one of these variables needs to be in the final model. In this case, CVD has been chosen to represent the correlated risk factors because it included the largest proportion of patients.

Variables removed from the adjusted model

The potential confounders removed from the model moving forward were:

- Smoking status
- Stroke
- Head/neck cancer
- Diabetes
- Second generation antipsychotics
- Influenza vaccination
- Pneumococcal vaccination

4.5.11 Adjusted odds ratios for refined model

Below are several versions of the refined model which further explore the effects of the different formulations.

Refined model 1: All co-variables *excluding* medicine formulations

Refined model 1 (Table 42) includes all co-variables to be included in the refined model but excludes medicine formulations. The presence of dysphagia was associated with more than tripling the likelihood of obtaining pneumonia whereas being a female was associated with almost halving the risk. COPD was associated with doubling the likelihood of a patient contracting pneumonia and having influenza was associated with greatly increasing the likelihood of also contracting pneumonia within the same year.

Table 42. Refined model 1 showing all refined co-variables but excluding formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.59	0.55 – 0.62	<0.001	0.02
Dysphagia:				
No	1			
Yes	3.57	3.19 – 3.99	<0.001	0.20
COPD*:				
No	1			
Yes	2.08	1.89 – 2.28	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.22	1.14 – 1.30	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.70	0.64 – 0.77	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.57	1.40 – 1.75	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	16.97	11.61 – 24.79	<0.001	3.28

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

Refined model 2: All co-variables *including* Solid formulations

Refined model 2 (Table 43) aims to explore the effects of solid formulations in more detail by adding this element into the refined model. Table 43 shows that patients that have recently been prescribed solid formulations may have be associated with a slight reduction in the likelihood of getting a diagnosis of pneumonia. The other odds ratios remained very similar to those reported in refined model 1 and therefore the presence of solid formulations does not moderate the effects witnessed by the other variables such as dysphagia.

Table 43. Refined model 2. Refined model of all co-variables and solid formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.59	0.56 – 0.62	<0.001	0.02
Dysphagia:				
No	1			
Yes	3.52	3.15 – 3.94	<0.001	0.20
COPD*:				
No	1			
Yes	2.09	1.91 – 2.30	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.23	1.15 – 1.31	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.72	0.65 – 0.79	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.58	1.42 – 1.76	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	17.01	11.64 – 24.86	<0.001	3.29
Solid formulation:				
No	1			
Yes	0.87	0.82 – 0.93	<0.001	0.03

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

Refined model 3: All co-variables *including* liquid formulations

Refined model 3 (Table 44) aims to explore liquid formulations further and similarly to refined model 2, the odds ratios of the co-variables do not seem to be moderated by the presence of liquid formulations. Table 44 shows how liquid formulations may be associated with independently more than doubling the chances of a patient contracting pneumonia.

Table 44. Refined model 3. Refined model of all co-variables and liquid formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.58	0.54 – 0.61	<0.001	0.02
Dysphagia:				
No	1			
Yes	3.33	2.97 – 3.73	<0.001	0.19
COPD*:				
No	1			
Yes	2.10	1.91 – 2.31	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.23	1.15 – 1.31	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.70	0.64 – 0.77	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.52	1.36 – 1.70	<0.001	0.08
Influenza diagnosis#:				
No	1			
Yes	17.30	11.82 – 25.32	<0.001	3.36
Liquid formulation:				
No	1			
Yes	2.28	2.01 – 2.58	<0.001	0.15

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

Refined model 4: All co-variables and mixed formulations

Combination of solid and liquid formulations was also prevalent amongst the study population so it was included in refined model 4 (Table 45) to determine this variable's corresponding effect. Table 45 shows no significant changes from any of the co-variables.

Table 45. Refined model 4 showing all refined co-variables and combination of solid and liquid formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.58	0.55 – 0.62	<0.001	0.02
Dysphagia:				
No	1			
Yes	3.57	3.19 – 3.99	<0.001	0.20
COPD*:				
No	1			
Yes	2.08	1.89 – 2.28	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.22	1.15 – 1.30	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.70	0.64 – 0.76	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.55	1.39 – 1.72	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	16.98	11.62 – 24.82	<0.001	3.29
Liquid + Solid formulation				
No	1			
Yes	2.61	1.99 – 3.43	<0.001	0.36

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

Refined model 5: All co-variables and both liquid and solid formulations

Refined model 5 includes both oral solids and liquids to determine whether there is moderation between the formulations. Table 46 shows however that neither formulations or co-variables ORs change substantially.

Table 46. Refined model 5. All co-variables and both liquid and solid formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.58	0.55 – 0.61	<0.001	0.02
Dysphagia:				
No	1			
Yes	3.30	2.94 – 3.69	<0.001	0.19
COPD*:				
No	1			
Yes	2.11	1.92 – 2.33	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.23	1.15 – 1.31	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.72	0.66 – 0.79	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.53	1.37 – 1.71	<0.001	0.086
Influenza diagnosis#:				
No	1			
Yes	17.33	11.84 – 25.37	<0.001	3.37
Liquid formulation				
No	1			
Yes	2.23	1.97 – 2.53	<0.001	0.14
Solid formulation				
No	1			
Yes	0.90	0.84 – 0.95	<0.001	0.027

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; # Diagnosis within 1 year of index date and including index date*

4.5.12 Sensitivity analysis

To test whether the formulation results reported in the refined models are independent to dysphagia, a sensitivity analysis was conducted. Dysphagia was firstly excluded from the model to determine any changes to the adjusted ORs of the formulations.

Next, each formulation was combined with the dysphagia variable to further explore what associations may be seen when formulations are added to those also with dysphagia. Table 47 summarises the models tested and any results of note. Full results can be seen in Appendix 14.

Table 47. Key results from sensitivity analysis

Model description	Adjusted OR results of note
Dysphagia excluded models	
Liquids included	No significant changes
Solids included	No significant changes
Solid and liquid combination included	No significant changes
Dysphagia + formulation variable*	
Liquids	Dysphagia (no liquids): 3.40 (3.02 – 3.83**) Dysphagia (+ liquids): 4.41 (3.30 – 5.90**)
Solids	Dysphagia (no solids): 3.42 (3.00 – 3.89**) Dysphagia (+ solids): 3.07 (2.45 – 3.84**)
Solid and liquid combined (comb.)	Dysphagia (no comb.): 3.54 (3.17 – 3.97**) Dysphagia (+ comb.): 6.40 (2.43 – 16.89**) ***

**Where 'No dysphagia' is the reference category; **P<0.001; ***Standard Error: 3.17*

4.6 Discussion

Currently this study is the first UK based study to analyse primary care data to identify factors related to pneumonia which include medicine formulations. There was a substantially higher proportion of males within the cases compared to in the controls and females were associated with almost half the risk of developing pneumonia. There were three times as many cases with dysphagia compared to controls and dysphagia was associated with over a threefold increase in the risk of developing pneumonia in all models.

COPD, first generation antipsychotics and influenza diagnosis were all associated with an increased risk of developing pneumonia to varying degrees whereas ACE inhibitors were associated with a reduced risk.

Solids were the most common formulation prescribed and the proportion of liquids prescribed in cases was double that of in controls. Liquid formulations and solid/liquid combinations were associated with an increased risk of developing pneumonia whereas solids prescribed on their own were associated with a slightly reduced risk.

In patients with dysphagia, the prescribing of liquid medicines was surprisingly associated with greatly increasing the risk of developing pneumonia whereas solids was associated with a negligible change in risk.

A statistician with previous CPRD experience was involved from the beginning which ensured a detailed a robust protocol was created, approved by ISAAC and followed throughout. The use of CPRD as a data source additionally provided access to a large dataset and enabled a robust nested case-control study to be performed.

Limitations to this project included the risks of consulting bias, where pneumonia is opportunistically diagnosed and diagnostic bias, where the GPs knowledge of the patient may alter the likelihood of making a diagnosis of pneumonia which were uncontrollable in this study. The accuracy and reliability of data (such as using the correct associated READ code) input by the GPs will not be known and was also uncontrollable but the selected codes for dementia, pneumonia each exposure included a broad range in order to try and minimise this. Additionally, patients diagnosed with pneumonia in secondary care rather than primary care may not have been identified in the study if the diagnosis was not passed to primary care and recorded. This could have potentially led to cases being misclassified as controls, which could have led to a weakening of any reported effects.

Medication related limitations include that this study method assumed that all patients were 100% adherent to their medicines and didn't account for missed doses or uncollected prescriptions. The study also assumed that orodispersible formulations were utilised by the patient correctly and were left to fully dissolve on the tongue and that dispersible tablets were dissolved fully prior to administration for both formulations to be categorised as 'oral liquids'. Furthermore, there was an inability to explore the full spectrum of prescribed medicines and formulations, which analysed may have provided differing results.

The length of time patients had been dysphagic or their stage of dementia could not be identified through this methodology and dataset reliably, which was another limitation to this study as this data would have been valuable to the research question.

Additionally, the thorough inclusion criteria for those eligible for pneumococcal vaccinations and the need for some to require booster vaccinations meant that identifying comprehensively all those eligible for the vaccination will be too complex for this particular study.

This method only provided an approximation for the socioeconomic status of patients. It was accepted that the data would not take individual circumstances into account and so the results needed to be interpreted with caution.

Similarly there were many patients in both groups with missing data for smoking which may have influenced the results regarding smoking status data.

A final limitation to this study was the use of the chosen study design. Although there are advantages to case-controlled studies, this design cannot definitively prove causalities of risk factors and confounders, but mere associations can be determined. Therefore,

although this study provides evidence of the associations between dysphagia, formulations and pneumonia, the true causes of pneumonia cannot be established.

In both groups the majority of patients were female. This is in line with an older study which reported that the rate of AD at 90 years of age was 81.7 (95% CI: 63.8 – 104.7) in women compared to just 24.0 (95% CI: 10.3 – 55.6) in men [195]. This may be due to women generally living longer than men [196] and so naturally more women will be diagnosed in total due to dementia generally becoming more prominent as age increases.

Although overall, fewer males seem to be diagnosed with dementia in the UK, there was a notable higher proportion of males in the cases (42.1%) compared to in the controls (29.9%). A 2-year prospective study reported similar findings with incidence rates of CAP increasing not only by age but were also higher in males (16 cases per 10,000 person-years) compared to females (9 cases per 10,1000 person-years, $p<0.0001$). Additionally, this rate increased for males ≥75 years to 87 cases per 10,1000 person-years and the incidence of *Legionella pneumophila* was 10 times higher in males [197]. Although the reasoning for this gender difference is unknown, this study reinforces the need for further investigations into why elderly men are more at risk compared to elderly women.

As with gender, much of the data in this study resembled that of the general population (such as the distribution of surgeries and the prevalence of common co-morbidities such as CVD, diabetes and COPD [198] [199] [200] and the low prevalence of smokers [201].

The small number of patients in both groups who had received an influenza diagnosis (including index date) could be a sign of the effectiveness of the annual influenza vaccination but approximately only 50% of patients in both groups were recorded to have had the vaccination the year before index date. The low diagnosis rates may not be representative of the population as due to the limitations described at the beginning of this discussion, patients with flu are advised to stay at home and are not likely to get a formal diagnosis by a GP. Therefore, the cases recorded are more likely to be only the severe cases reviewed by GPs or hospitalised due to complications.

The current prevalence of dysphagia in PWD has up until now been unclear. This study therefore provides data on the approximate prevalence of dysphagia being approximately 4.15% across all sectors which is considerably lower than the estimation of 45% in institutionalised patients [45].

This study has reaffirmed the associations that the risk factors introduced in section 1.6.2 have to pneumonia in not only the elderly, but also within a cohort of patients with dementia, which in some cases had not been previously tested.

The slight association of smokers and ex-smokers with an increase the risk of developing pneumonia was not unexpected as it was a known risk factor and has a clear underlying pathophysiology (see chapter 1).

The high associated risk of developing pneumonia in PWD and COPD is understandable (as touched on earlier with smoking) for two reasons. Firstly, the association of COPD with pneumonia is already well documented. Torres et al. [202] describe how patients over the age of 65 years old with mild lung disease were shown to be twice as likely to have community acquired pneumonia (CAP) and those with severe lung disease to be eight times more likely.

The large OR and 95% CI calculated in regard to influenza diagnosis, although statistically significant should be interpreted with caution due to the large standard error which was probably due to the small numbers of patients who had a record of influenza in their records. Further work may be required in this area using more appropriate methods for identifying patients with influenza in secondary and primary care and additionally including those within the community who do not get an official diagnosis. Only by including all patients will the true association of PWD with influenza and developing pneumonia be effectively determined. This work could potentially be another case-controlled study but one where patients are recruited prospectively and identified by screening against a checklist for influenza and pneumonia symptoms and having a procedure in place for the study to have the ability to send off samples in order to accurately diagnose the screened patients (although this could be costly). People with suspected influenza are recommended not to visit their GP surgery and to stay at home. Consequently, the recruitment methods to identify such participants would need considerable thought.

The presence of a pneumococcal vaccination either within 1 year or at any other time was not strongly associated developing pneumonia, which ties in with the data reported in chapter 1 where marginal effectiveness was seen in elderly populations [52, 53].

Of the 3 medicine groups explored for their association to pneumonia, ACE inhibitors were the most commonly prescribed medicine, with more being prescribed in the control group. Although results have been conflicting regarding the role of ACE inhibitors with pneumonia

[54, 56], the results from this study support the results by Shah et al. [54] who reported their association with a reduced risk of hospitalisation for pneumonia (Relative Risk: 0.52, 95% CI: 0.36 – 0.76).

These results do suggest that there may be a true association between ACE inhibitors and pneumonia but due to the small effect seen in this large sample, further exploratory work should be undertaken to determine the true nature of this association.

The increased risk of developing pneumonia associated with the use of first generation antipsychotics such as haloperidol, flupentixol and pericyazine is also in line with other studies such as Knol et al. [71] who reported an adjusted OR of 1.60 (95% CI: 1.3 – 2.1) with antipsychotic use within an elderly population.

This study also builds upon a Finnish study who reported how there was an increased risk of pneumonia in people with AD when initiated on anticholinergics (such as antipsychotics) (OR: 2.68, 95% CI 2.15 - 3.34) and was increased among those using both acetylcholinesterase inhibitors and anticholinergics (OR: 1.53, 95% CI 1.41 - 1.66) [203].

Cases had a much higher proportion of patients with dysphagia which is not unexpected considering that there is a wealth of literature which describes how dysphagia can cause aspiration which in turn can introduce pathogens into the airways and cause AP [45, 47, 204].In this study, dysphagia was consistently associated with over a threefold increase in the likelihood of developing pneumonia whichever model it was placed in. This is in line with the narrative review which also reported that there was a 3-fold increase in pneumonia risk among stroke patients with dysphagia [48]. The limitation of being unable to identify the severity of dementia denies us the opportunity to explore this theory further but does provide evidence that dysphagia in dementia is prominent in those who develop pneumonia compared to those who do not.

There is a paucity of studies which have been conducted in purely a dementia cohort and so this study provides new and exciting data regarding the prevalence and associations of dysphagia to pneumonia in PWD.

The distribution of the formulations of the five medicines in both groups was as anticipated. The higher proportion of liquids in cases may be due to those with pneumonia having experienced aspiration pneumonia due to swallowing difficulties caused by the severity of late stage dementia. These patients may therefore have been prescribed liquid

formulations in order to attempt to manage the safe medicine administration in dysphagia and dementia.

No previous research has been undertaken which assess specific medicine formulations and the development of pneumonia so the result of an increased risk of developing pneumonia being seen to be associated with liquid formulations was novel. This controversial result (considering liquids are often prescribed when swallowing problems are found) may however be explained by the fact that dysphagia was not further categorised (i.e. by type or severity). Some patients will have had a type of dysphagia where they were not at risk of aspirating whereas those with a more severe dysphagia or pharyngeal dysphagia will be more likely to aspirate in the first place and will therefore be more likely to have been prescribed liquids to counteract the risk of problems swallowing solids.

It should however also be noted that the association between liquids and pneumonia could also be partly due to some liquids not being the correct consistency for the patients and this also causing aspiration and AP. Patients should individually be assessed for their medicine formulation needs and changes made (e.g. use of thickeners) where needed.

4.7 Chapter conclusions and logic model development

This nested case-controlled study has confirmed that many well-known and well researched risk factors in the elderly (such as diabetes and CVD) are also associated with developing pneumonia in PWD, with dysphagia and COPD showing the largest associations. The management of these potential risk factors (such as COPD) and early detection of dysphagia should therefore be considered for a future intervention and have been included into the logic model (Figure 10).

This study also reported that antipsychotic use in PWD was associated with developing pneumonia, which ties in with why they were targeted in several of the interventions found in the narrative review in Chapter 2.

This study also therefore links with Chapter 2 as both studies showed results that suggest how PWD are often prescribed multiple medicines (such as antipsychotics and medicines for dementia) which are tackling a range of co-morbidities.

This study has also provided new evidence regarding the prevalence of dysphagia in PWD and the potential links between dementia, dysphagia and medicine formulation. Importantly, the use of liquids was calculated to be associated with greatly increasing the

chances of developing pneumonia compared to other formulations for PWD. This could be due to the liquid consistency not being appropriate for the need of the patient or it may be a proxy for the severity of the dysphagia. Reviewing the appropriateness of PWDs medicine formulations is also therefore an important element to consider including in a future intervention and has also been added to the logic model (Figure 10).

4.8 Next steps

Now that we have a greater understanding of what other specific aspects may be of value in a future intervention in order to reduce the chances of PWD developing pneumonia and therefore becoming hospitalised and their dementia potentially deteriorating further, we now need to look at the design of the intervention from the perspective of the service user. It has not been truly documented how PWD living in the community manage their medicines currently, nor what their preferences may be for a community pharmacy intervention. The next study will therefore concentrate on what PWD may find of benefit from their perspective in a future intervention and this is explored in the next chapter (Chapter 5).

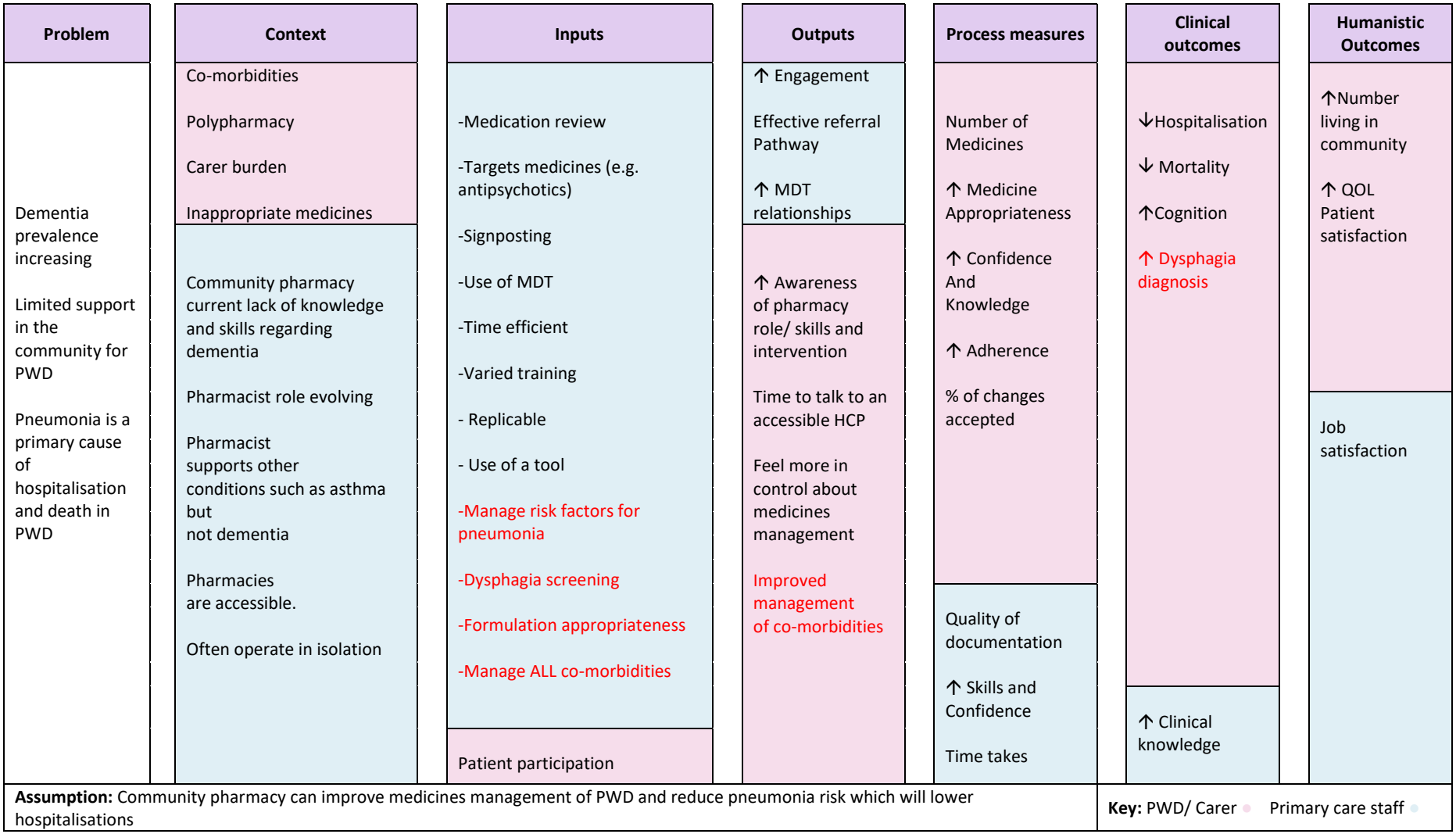

Figure 11. Developing logic model after CPRD study

Chapter 5.

Observations of how people living with dementia manage their lives and their medications in their homes

5.1 Chapter overview and introduction

Chapters 2 and 4 have provided a variety of elements which would be relevant to include in a future community pharmacy intervention. However, neither of these study designs have provided any information on how PWD who live in the community currently manage their medicines. Exploring how PWD currently manage their medicines would build on the knowledge gained in the previous chapters in two ways. Firstly, it would potentially provide new insights into how PWD may adapt their day-to-day life and surroundings in order to manage their medicines, which may be beneficial to other PWD, when shared as part of a pharmacy intervention. Secondly, it may highlight difficulties that some PWD face with managing medicines at home, which could be potentially be overcome with further support from a community pharmacy intervention.

To ensure that a future community pharmacy intervention included aspects as relevant and beneficial to PWD as possible, it was therefore vital to design and conduct a research project which directly explored how people with dementia, were organising their lives in the community and how they managed their medicines.

This chapter describes an observational study, where I visited ten homes of PWD (with and without informal carers) to explore how they currently managed their medicines.

5.2 Aim and objectives

Aim

To observe and explore how people with mild to moderate dementia and the informal carers of people with mild to moderate dementia who may support them, manage their lives, with particular attention to how they manage their medicines to inform the development of a new primary care intervention. The activity of managing medicines would be likely to involve:

- Access to medicines. This may include how the medicines were ordered, collected and stored
- Medicines organisation and medication administration by either the carer or the person with dementia
- How medicines were initiated, stopped and intermittently reviewed.

Objectives

In relation to ordering, organising and administering medicines (collectively described as ‘medicines management’), the objectives were to:

- Describe how patients with mild to moderate dementia currently manage their medicines within their homes.
- Identify any related challenges patients with mild to moderate dementia and informal carers may face regarding the safe and effective management of medicines in the home and identify any methods they use to overcome the challenges.
- Describe the views of people living with mild to moderate dementia and their informal carers about the current role of their primary care healthcare professionals in relation to how they manage their medicines.

5.3 Methods

5.3.1 Study design

To gain an understanding of how PWD who live in the community and their informal carers manage their medicines, I needed to use a study design which would provide me with the most accurate and detailed information about how they did this. PWD are at an increased risk of recall bias due to the dementia affecting their memory and so a study design which allowed me to see first-hand how PWD manage their medicines was needed. I also wanted to use a study design which would allow the participants to feel comfortable about talking about sensitive information as I was aware how some participants may feel embarrassed when talking about their medicines or experiences with their dementia. Furthermore, I needed to use a study design that ensured that no unnecessary burden was placed on the potentially vulnerable participants and that participants were not involved any longer than required. This meant that I preferred a study design which allowed me to spend time with PWD, observe them with their medicines and ask them questions about their arrangement, in the context of their own homes for short periods of time. Study designs considered included phenomenology, grounded theory and ethnography.

Phenomenology aims to describe the meaning of a lived experience of a phenomenon, such as managing medicines whilst living with dementia, whilst grounded theory consists of the development of new theory about a phenomenon which can then be applied in healthcare to alter how existing problems are approached [205].

In phenomenology, the interest is in common features of the lived experience. I.e. common features of living with dementia and managing medicines. Seeing as I want to explore how a variety of PWD manage their medicines and my aim is not necessarily to find only the common features for how medicines may be managed [206], this study design may not be

the most appropriate. Additionally, the optimum method for data collection in phenomenology is unstructured one-to-one interviews, which tend to start with a question such as 'tell me about your experience'. Such interviews can enable the interviewee to draw a vivid picture of the experience, which leads to understanding of shared meanings [207]. However, using such an approach with PWD may lead to inaccurate or incomplete accounts being shared due to the memory loss associated with the dementia. Additionally, I may not be able to place their experiences into context or see their medicines first-hand which could have limited my understandings of how and why PWD and their carers do certain things with their medicines. Silverman has actually argued that interviews are overused in qualitative research and that their critical adoption provides little more than anecdotal insights, giving researchers a false sense of authenticity [208].

Using phenomenology and individual interviews were therefore inappropriate for exploring how PWD manage their medicines in the home.

Grounded theory is appropriate when the study of social interactions of experiences aims to explain a process (such as the process of managing medicines. It consists of cycles of simultaneous data collection and analysis, where analysis informs the next cycle of data collection [209]. Grounded theory can use a range of data collection methods from semi-structured interviews to focus groups to reviewing diaries. The cyclical nature of this study design means that the study is at risk of going off on a tangent as the research question evolves with the emerging theories. For this study, although the main aim is to comprehensively explore how and why PWD manage their medicines the way that they do, I do not intend to create theories from the data. Grounded theory is therefore not the appropriate study design to use.

Focus groups are a method used in many study designs that is often used for exploring people's knowledge and experiences on a certain subject [210]. Focus groups can be an efficient method for data collection by providing a wealth of information on views from a wide group of participants in a small amount of time as the participants are encouraged to talk to one another, ask questions, exchange anecdotes and comment on each other's experiences and points of view. Focus groups can also encourage contributions from people who often do not voice views or who are reluctant to be interviewed on their own for various reasons (such as feeling intimidated or isolated) in individual interviews [210]. There are four disadvantages for using this approach to explore this study's research question:

1. Focus groups could introduce recall bias as they may discuss issues which include sharing experiences retrospectively. This means that the information shared may not be accurate or may be incomplete.
2. Due to the sensitive nature of the research, the participants may not feel comfortable in a group setting and so may not share as many views or opinions as they may if they were on their own or in their own homes.
3. The participants could become confused during the focus group and become agitated or stressed, which could be difficult to manage in a group setting.
4. Focus groups are conducted in a neutral, non-domestic space rather than in a person's home. This means that I would not be able to collect direct data on how PWD manage their medicines.

Focus groups were therefore not an appropriate method for exploring how PWD manage their medicines at home.

An ethnographic study design was a potentially appropriate approach to use, as this design enables detailed understanding of how participants act in a particular cultural context [211] by using data collection methods such as formal and informal interviews and participant observation. Using this study design would allow me to observe, in context how PWD manage their medicines and allow me to immerse myself in their everyday lives. Traditional ethnographic studies are based on a researcher's long-term exposure to a certain culture or multiple visits to participants and involves the scientific description of groups of people who have something in common (such as all living with dementia). However, the focussed research question of exploring how PWD manage their medicines meant that this study did not require such lengthy exposure and could place unnecessary burden on participants with dementia. A traditional ethnographic study design was therefore also not appropriate. Focussed ethnography, a sub-form of ethnography, is characterised by short-term field visits, problem-focussed, context specific, involves a limited number of participants and focuses on a discrete community where participants usually hold specific knowledge [212, 213]. It has emerged as a promising method for applying ethnography to focus on a distinct issue or shared experience in cultures or sub-cultures in specific settings rather than throughout entire communities and has been shown as useful in several nursing research studies [213]. One example is Tzeng et al. [214] who described the ways psychiatric nurses (n =18) provided care for and responded to dilemmas associated with caring for suicidal patients by conducting participant observations and using field notes. As seen in this study, focussed ethnography enabled a specific problem to be evaluated in a specific field with a

small sample and features close observations of the participants in the location, asking questions to gain an insight into current events to gain a complete understanding of people, places and events [215]. Using focussed ethnography would allow me to observe PWD and their carers within their own environments and provide me with the opportunity to observe how they manage their medicines in context. Focused ethnography would allow me to keep the observations short and focussed which should be more manageable for PWD and their carers and lead to a reduced risk of the participants becoming anxious, stressed or confused.

For these reasons, this study adopted a focused ethnographic approach, which would use the data collection method of short, singular observations.

5.3.2 Photographs

Photographs of certain objects or aspects of an observation can be a useful data source for studying cultural patterns [216] as they provide a visual representation for contextualising and placing what the researcher observed. This can not only make it easier for readers to interpret and visualise the type of situation being described, but also provides validity to the study as it can be triangulated with the descriptions in the transcripts and expanded accounts.

I took up to three medication related photographs per observation, ensuring that they did not include any patient identifying features and remained anonymous.

5.3.3 Setting

This study is exploring how PWD and their carers manage their medicine at home and so it was important that the observations were of what happened in participants' homes where their management of medicines could be observed in context of the participants in their homes and so I had the opportunity to see and discuss elements of their medicines.

The study aimed to explore medicines management by PWD. This would include observing how participants take their medicines. Therefore, observations were planned to take place at a mutually agreed time which was also around the time which the PWD took their medicines. As the study got underway and it became clear that having the observations during times when medicines were taken often not possible where medicines were often being taken when the participants were in bed, the protocol was amended accordingly. Following this amendment, when it was not possible to observe during the times that

medicines were taken, the observation took place at any time the participant suggested and when I was available.

Where the observation time included the time that people would usually take their medicines, I arranged to arrive about one hour before the time that they said they would be taking them. This allowed time for the observation to be as natural as possible and for me to further develop rapport with the participant which should encourage the participant to be more at ease and open with me. The rapport which I built with the participants encouraged participants to behave openly with me in relation to where medicines were stored in their homes, how they took their medicines, their frank opinions of their surgeries and pharmacies and in describing how they managed their day-to-day lives whilst living with dementia. This led to the data collected providing detailed accounts of participants' words and actions and allowed me to gain a more deeply contextualised and credible understanding of how they managed their medicines.

The majority of the observations took place focused in one specific location within the home. However, when the participants were discussing topics relating to medicines or needed to take their medicines, I would follow and 'shadow' the participant(s) as they moved around the home to either show me certain things such as their medicines or their repeat slips or for me to watch the participant get out and take their medicines. In some instances, the participants would tell me to follow them or spontaneously invite me to see something they were talking about. In other instances, I would take the initiative to ask the participant whether they saw it as okay for me to follow the participant or to see in person, what object or arrangement the participant was talking about. I did not enter private areas such as bathrooms and bedrooms unless explicitly invited or granted access by the participant. Having the ability to shadow the participants during certain times of the observation allowed me to see in context exactly and in detail how certain procedures were done (such as preparing and taking the medicines) within the home which, with other methods, would not have been possible.

5.3.4 Study Participants

5.3.4.1 *Inclusion Criteria*

The intended final outcome of the overall research project was to develop a community pharmacy intervention for people affected by dementia who live within the community. To ensure that the results of this observational study would be relevant to the overall project

outcome, participants were required to have a diagnosis of dementia, live in the community either alone or with someone who was their informal carer and who may access their local community pharmacy for them.

The inclusion criteria for this study were therefore:

- **PPs were living in the community and in their (or their informal caregiver's) own home** - Assessed during the screening process (see below) by the nurse to ensure the participant would be relevant and eligible to the study.
- **People living with dementia who were more likely to access their local pharmacy** – Participants had been assessed by the local NHS Foundation Trust (NHSFT) memory clinic and had a diagnosis of mild-moderate stage dementia. This was because this is the stage of dementia a patient will most likely be accessing and using their community pharmacy.
- **PPs were able to meet me prior to the observation in a safe space** - PPs required a new dementia medicine follow-up visit with an NHSFT community mental health nurse. This meeting was deemed an appropriate opportunity for me to discuss the study with PPs as they were more settled with their dementia diagnosis and new medicine and ensured that I was meeting the PPs somewhere mutual and safe for both the PP and myself due to the nurse also being present. This also increased the likelihood of a PP being more receptive to the study and a better rapport being built with me.

5.3.4.2 *Exclusion Criteria*

The exclusion criteria originally planned included the following:

1. Most of the medicines were taken at night just before the participant went to bed or very early in the morning, which could be experienced by both the participant and I as too unsocial hours to visit. This was because the study was exploring all aspects of medicines management which includes the taking of the medicines.
2. They lacked capacity. (This information is initially sought from whether the PPs had capacity to complete the NHSFTs 'Data Protection Act 1998 – Consent for

disclosure' form). This was to ensure that only those PWD who had capacity were included and so fully understood the study details.

3. They had formal carers. This is because formal carers may have to follow certain guidelines within their company and would not manage their client's medicines as an informal carer may, who would be more likely to visit and obtain support from their community pharmacy.
4. They had not provided consent for their information to be shared with other professionals for research purposes on the NHSFT 'Data Protection Act 1998 – 'Consent for Disclosure' form completed for all patients. This was to ensure that only PPs who were willing to take part in research or have their details shared with me did and those that did not had their right to confidentiality within the NHSFT respected.
5. They were unable to understand English in verbal or written form or were unable to communicate effectively due to a disability or language barrier. This was to both ensure that I could determine effectively that the PPs fully understood the study as well as conduct the observation effectively.

5.3.4.3 *Amended Exclusion Criteria*

During Observation 2, there was no observing of medicine administration due to the medicines being administered at bed-time. However, the observation contained a wealth of useful and relevant data and it was decided that participants should still be eligible regardless of when medicines were administered. A request to delete exclusion criteria point 1 was submitted to the HRA which was agreed 05/12/2017 (Appendix 15.1) with approval from the hospital trust following on 29/12/2017 (Appendix 15.2).

5.3.5 Recruitment

Recruitment sites

A recruitment site was required which had access to large numbers of people living with mild-moderate dementia who tended to live at home in the community. Recruiting from such a site would enable the study to meet its ideal sample size within the time and allow the study to include a more diverse population which in turn allows for more comprehensive data.

Participants were recruited via two sites in a local NHS trust which specifically provides services to patients suspected of having dementia which includes:

- Assessment of mental health and memory problems.
- Diagnosis of mental health and memory problems.
- Treatment of memory problems.
- Monitoring of treatment plans, which includes new medicine follow-up visits with a community mental health nurse.

Screening

The community mental health nurses (abbreviated to "nurses" from here on) were the initial recruiters to this study as they had access to information which was required as part of the screening process and they would be able to introduce me to PPs at a future medicine follow up meeting.

To ensure the inclusion and exclusion criteria were adhered to, and that only eligible PPs were approached by the nurse and included into the study, a recruitment checklist (Appendix 16) was created. Prior to the study commencing I went through the checklist in detail with the nurses and provided copies for them to place in areas of their office that could be easily accessible.

When the PPs were contacted by the nurse to arrange their new medicine follow-up visit, the nurse used the prompt paragraphs on the checklist sheet to introduce the PPs to the study and ask if I could meet them during the follow-up visit to provide them with more information. The nurse confirmed that their PPs had capacity at this stage by checking their understanding of what was going to happen. I remained in close contact with the nurses during this stage to maintain motivation and recruitment.

Confidential participant summary sheets

If the PPs provided verbal consent to the nurse for meeting me and finding out more about the study during the initial contact with the nurse, the nurse then emailed me to inform me that they had recruited a new PP. The nurse then completed a confidential participant summary sheet (Appendix 17) which included basic personal information of the PP such as name, address, date and place of next appointment. The nurse then placed the summary sheet in a folder labelled as 'new potential participants for managing medicines study' which was then stored in a secure filing cabinet at the research site, within a locked office.

Transfer of data

When I received an email from the nurse regarding a new PP, I then visited the research site to transfer the details completed by the nurse on the confidential summary sheet (such as: participant reference number, address, independent/dyad, appointment date, time and location) onto a password-protected Microsoft Excel spreadsheet (with columns for each of these features) on a password protected laptop. The confidential summary sheet was then updated with a reference number and placed into a folder clearly marked as 'collected potential participants for managing medicines study' which was stored in the same secure area as the previous folder.

Meeting PP

I attended the follow-up appointment with the nurse at either the clinic or at the PPs home to be introduced by the nurse to the PP. Having the nurse introduce me in the first instance was important as the PP was likely to trust their nurse due to their profession and would be more likely to therefore trust a colleague of theirs (such as myself) if the nurse is seen to be happy to introduce me to the PP. This could then increase the likeliness of the PP being receptive to me in the meeting and being more likely to take part in the research.

This meeting also ensured participants met me before an observation took place with them. This allowed me to explain the research in more depth, answer any questions and to help build rapport between myself and the participants. This is an important factor for successful observations because rapport encourages participants to talk freely about their particular 'culture' and allow researcher and participants to exchange information more freely [217] and the participant to feel more at ease to ask questions themselves, comment unrestrictive or express their need to stop the observation.

At the beginning of the follow-up appointment, the nurse firstly explained to their patient that the first half of the meeting would be about their new medicine and then they would pass over to me for the second part to discuss more about the study. I then observed the follow-up appointment between the nurse and the PP ensuring that I did not disturb the main reason for the appointment.

Once the community nurse has completed their activities within the appointment, the nurse handed over to me. Dependent on the nurses' schedule, sometimes the nurse remained in the room to listen and sometimes they left the room in order to do other tasks.

I explained in lay terms the reason for the study and what it involved. If the PP seemed interested, I provided and went through the participant information pack with them which included: a cover letter (Appendix 18), a participant information sheet (Appendices 19-21), a consent form (Appendices 22-24) and a stamped addressed envelope. During this process, I also checked that the PP still had capacity by using personal judgement and the ability for the PWD to relay their understanding of the project back to me. After answering any questions, the research pack was then left with the PP and I reassured them that they were welcome to contact me at any time if further information was required. PPs were instructed to take some time to think about the study before completing the consent form but to post it back to me within 7 days. Due to the participants being people who were living with dementia, there was the possibility that during those 7 days PPs that were interested in the study and seemed happy to take part may have forgotten about the paperwork and not post a consent form back to me. Therefore, during the meeting, I also ensured that the PPs provided her with a contact telephone number if the nurse hadn't already done so and was later added to the confidential summary sheet and Excel spreadsheet. This number was used to remind the PPs of the study and to post consent forms back to me if they were not received within 7 days of this initial meeting. When reminder telephone calls were conducted, I reiterated that the PPs were not obligated to take part in this study, could withdraw at any time and if a consent form was not received in a further 7 days then they would not be contacted again.

Setting up observation appointments

I followed up returned consent forms via telephone. During the telephone call, I discussed with the participant when the PWD usually takes their medicines and together, agreed a mutual time, date and suitable location for the observation which was socially and practically acceptable for both myself and the participant.

A reminder letter (Appendices 25 and 26) was posted along with a photocopy of the signed consent form to the participants 7 days before the scheduled observation to provide a visual reminder.

I then conducted a reminder telephone call on the day before the scheduled observation to ensure that the participants would still be home and happy for the research to take place the next day. Due to dementia symptoms and capacity being able to fluctuate, during this telephone call, capacity was checked once again to ensure the participant still met the

inclusion criteria. This was done by my judgement of the participant's involvement in the conversation and ability to understand and reiterate what was discussed during the call.

The above process is summarised as a flowchart in Appendix 27**.**

5.3.6 Observation

When a researcher truly respects the people they are observing, the participants are more likely to participate in the research context in a way that maximises the success of the project. I therefore ensured that I continued to build rapport during the observations and follow the ethical principle to respect the rights, lives, attitudes and opinions of the people that I was studying [218].

This section describes in detail how the beginning of the observations, the observations themselves and the end of the observations were conducted and how this ethical principle was followed.

Beginning the observation

I arrived at the participant's home at the mutually agreed time and introduced myself on a first name basis attempting a friendly and warm manner. This involved making good eye contact, open body language and using an enthusiastic voice tone to convey how happy and grateful I was to be at the observation. This was to help ensure the participant was as relaxed as possible and to convey that I wanted to be at the observation and that I was grateful to the participant for allowing me into their home. I confirmed with the participant that they were the named participant and checked whether they were still willing for me to enter the home and spend some time with them. Having a mutually agreed time, ensuring the participants were relaxed and gaining consent for me to enter the home helped ensure that the rights and the lives of the participants were respected.

Once I had entered the home, I took part in conversation led by the participant(s) about such subjects as the weather and how my journey to their home had been in order to ensure that the participants felt relaxed with my presence and to further build rapport. This consequently ensured that the lives of the participants were respected. Verbal consent was sought to begin the observation and an audio-recorder sequentially turned 'on'. This process aimed to be light and conducted in a conversational manner in order to allow the setting to continue as naturalistically as possible.

During the observation

Given my aim of exploring how PWD manage their medicines in their homes, it was important for me to be able to communicate with the participants during the observations, so that I could ask them in context how, where and why they did certain things (such as organising and administering their medicines) and ask them to show me certain objects (such as their medicines) or their usual daily routines. I wanted my communication with the participants to fit with everyday conversation and be free flowing to help build rapport and rather than making the observation feel formal or awkward. I hoped that this would make the participants feel more at ease and be more likely to share information and views with me. I also wanted to be able to ask the participants questions and to discuss a variety of focussed topics on an ongoing basis and as part of this flowing interaction so that I could clarify certain points or ask for further expansion on areas of particular interest at the time. Being able to have this level of interaction would make it more likely that I could gather detailed, accurate and context-relevant data on how PWD and their carers manage their medicines within their homes, to enhance the rigour of this study.

Although I planned to observe the participants undergoing their everyday routine, I would not participate in tasks myself such as cooking, cleaning or preparing the medicines for someone to take but if I was offered a drink I would accept the offer where desired.

There is a continuum of research observer stances which I could have taken during these observations which includes non-, passive, moderate, active and complete participation [219] (see Table 48) but only the moderate participation stance would have allowed me to both observe and interact with the participants on a one-to-one basis in a way which would enable me ask questions where needed and therefore gather accurate and comprehensive data.

At one end of the spectrum is the ‘complete participant’ stance. To take this role I would have to become one of the members of the group and conceal my research role, to avoid disrupting normal activity. This role would have allowed me to truly immerse myself in the culture and experience for myself how medicines are managed at home, but it would have meant that I would have needed to become a carer for a PWD in the community. This would not have been possible and there are ethical questions regarding knowingly deceiving participants [220].

At the opposite end of the spectrum is the ‘complete observer’ or, ‘passive participation’ observer. In this stance, I would be completely hidden from view while observing, or in plain sight in a public setting where the public are unaware of being observed by me [220].

This stance would mean that I am not being obtrusive or causing the participants any undue stress or anxiety and the participants would be unable to modify their behaviour. However, this stance would have been difficult to use in practice due to the setting being in peoples' homes and secondly, the data I could gather would be limited as I would be unable to ask them questions about how or why they do certain things or ask them to show me specific items or places so that what they are saying can be put into more context.

Table 48. Continuum of participation stances

Non-participation	Cultural knowledge is acquired by observing phenomena from outside the research setting such as by reading diaries or watching television
Passive participation	I act as a pure observer, do not interact with the participants who may be unaware that they are being observed
Moderate participation	I'm present at the scene of the action and have limited participation. May involve a structured observational framework
Active participation	I engage in almost everything that the participants are doing as a means of trying to learn the cultural rules for behaviour
Complete participation	I temporarily become a member of the group being studied

Midway on the continuum is the 'moderate participation' stance. This stance would allow me to be present in the observed environment and have some participation with the observants. Using this stance would allow me to see their routines and certain objects in context and allow me to ask them further questions where desired and is therefore the stance of choice. Being able to ask the participants questions to gain further information in relation to their routines, medicines or certain objects and see how they managed their medicines in the context of their own homes would provide a wealth of data which should be accurate and comprehensive.

Taking the 'moderately participating', would mean that the participants were aware that I was observing them. Being a community pharmacist, I was aware throughout the study that there was a risk of the participants modifying their behaviour and/or usual routines for my visit which could lead to a form of researcher-researched bias [221]. I was aware that due to my profession and the main focus of this research being about their medicines, participants may have consciously or even unconsciously felt a need to gain my good professional opinion. For example, they may have reorganised their medicines prior to my visit, or taken their medicines slightly differently to usual during the visits. I tried to counteract these risks of bias by ensuring I built rapport with them before and throughout the study and reinforced to them that I remained supportive of and interested to observe their usual routines, whatever these were.

Where possible, condensed notes or jottings were recorded onto an observation guide (Appendix 28). The participant(s) were asked beforehand if they were comfortable with me 'jotting a few things down whilst I am with you'.

There were instances when I observed the use of a discussed physical object (such as a dossette box or reminder method) or observed a particular environment within the home (such as a medicine storage area), which may be associated with how PWD manage their medicines within their homes. These objects or environments are difficult to convey in words and so in these instances I would ask permission from the participants to take an anonymous photograph.

Seeking permission from the participants to jot information down and to take photographs ensured the participant's rights were protected.

Ending the observation

I brought the observations to a close when the participants indicated to me that they had shared all of their information with me in regard to how they managed their medicines. This was usually by such phrases as 'is there anything else you would like to know?'

To show my gratitude to the participants and ensure that they were aware of they had made a welcome contribution to my study, I usually explained to the participant(s) that I had found the observation most helpful, had observed enough of their usual routine to build my knowledge of what was happening, did not want to take up any more of their time and clearly thanked them for being participants in the study.

5.3.7 Sampling

5.3.7.1 *Sampling technique*

Those affected by dementia and living in the community all live with different circumstances and will therefore manage their medicines in different ways. In order to answer the research question comprehensively, it was important to include as many different people and circumstances as possible. A sampling technique was therefore required which allows for the inclusion of a range of people (such as age, gender and carer status) and circumstances (such as number of medicines) and the ability to purposefully choose participants from across this spectrum.

Heterogenous, purposive sampling involves purposefully selecting a range of participants from across a broad and varied spectrum. PPs could be selected based on their potential contribution to ensuring that the full range and extent of how medicines are managed at

home were represented [222, 223] and I therefore chose this sampling technique for my study.

5.3.7.2 *Sample size*

A specific and precise sample size could not be pre-determined as data collection would need to continue until the phenomenon was fully investigated, which would be when no new additional interpretations or themes emerge from the observations of this participant i.e. when data saturation is reached [224].

Although there was no way to predict the sample size required, I needed to have an approximate figure in mind to estimate the potential feasible length of the study.

I gathered data from the nurses on the average number of patients referred to them each week and the average number of these that had mild-moderate dementia and lived at home. From this data I estimated that one of the recruitment sites for this study received an average of 4 new referrals per week to their medicine consultation service of which approximately 80% would have a mild – moderate dementia diagnosis.

Based on this knowledge and assuming that not all new referrals would meet the inclusion criteria or wish to participate in the study, it was possible to estimate that from this site, that one to two participants may be recruited per week.

The second site was a larger recruitment site where on average 180 patients were seen by three memory treatment nurses per month. Assuming that the demographics were similar to the first, smaller site, it was estimated that 2-3 participants may be recruited from this site, providing a total of 3-5 new participants per week to the study.

The recruitment time required to reach up to 20 observations would therefore be four to seven weeks and so fieldwork would require up to eight weeks.

However, I appreciated that the recruiters would have high pressure, busy schedules which greatly increase with staff holidays or illnesses. To minimise further stress to the recruiters, provide a more realistic timescale for the study and allow for PPs dropping out, I planned a total of 20 weeks for completing recruitment and observations. This was feasible as fifteen to twenty observations were likely to be required to reach data saturation. This could be completed during a 5-month timeframe.

5.3.8 Methods of recording observations

The observations were recorded using five key methods: condensed accounts or fieldnotes; expanded accounts of the observation; photographs; anonymised transcripts of the observations; and a research diary.

Condensed accounts/ fieldnotes

I made fieldnotes during the observations where possible, using an observation guide (Appendix 28) that I had designed for this study and setting then tested, to focus on aspects of interest to the research question. During the observations, jottings taken included: key quotes, key word lists, medicines observed and drawings of particular rooms or situations. Where jottings were not possible during the observation, they were written down as soon as I was able such as in the car once I had left the home to ensure that as much data was captured as possible [225].

Expanded accounts

As soon as was possible, I expanded the condensed accounts into anonymous detailed accounts of the observation, which were written in chronological order. This included information regarding immediately before and after each observation.

Photographs

I took up to three photographs per observation of objects which I deemed of interest to the research question. These were transferred into the expanded accounts to help convey some of the descriptions within.

Transcripts

Each observation was recorded with the use of a Dictaphone. I took two Dictaphones to each observation and tested them before I reached the observation site. This ensured that if one did not work, recordings could still take place. The recorder remained close to meat all times.

I then transcribed each audio recording ensuring that the transcripts were anonymised.

Research Diary

I maintained a research diary throughout the study which I used to document:

- Pre- and post- observation reflections. I recorded my feelings, current theories, memos or thoughts from each observation and whether they went how I expected

them to. The diary also provided a space where I could be reflexive about the observations by being critical, honest and open about the research process and my researcher-researched relationships. As part of this, I was able to document how the participants interacted with me and whether I felt they may have modified their behaviour at all which was then useful to keep in mind during the analysis of the observations.

- My study developments in terms of recruitment. When recruitment was particularly difficult, I used the diary as a place to write down my thoughts and potential solutions. This helped me to gather my thoughts and be able to concentrate more clearly on the analysis of a previous observation or prep for the next one.
- The ongoing data analysis. I documented my thoughts and questions in the diary whilst I was coding along with my emerging themes. This helped to shape the emerging themes into the final themes reported in this chapter.

5.3.9 Ethical considerations including consent and confidentiality

This study gained approval from the Health Research Authority approval, Research Ethics Committee and the local NHSFT on 11/08/2017 (Appendix 30), 08/08/2017 (Appendix 31) and 20/09/2017 (Appendix 32) respectively.

The four ethical principles non-maleficence; autonomy; justice and beneficence [226, 227] were considered in terms of the specifics of this study to ensure that the study was conducted ethically and to reduce the risk of harm to myself and the participants.

5.3.9.1 *Non-maleficence*

'Above all, do no harm' is among the most quoted principles in health care ethics [226] and it was important for procedures to be implemented to ensure that neither the participants nor I were harmed in this study. Additionally, the participants of this study were vulnerable due to the presence of dementia and so further safe-guarding procedures needed to be considered. The procedures implemented to reduce risk of harm to both the participant and I are outlined below.

Risk of harm to participant

I was mindful that the participant(s) could become confused or distressed and that they may have been less able to communicate their feelings to me. I reduced these risks in the following ways:

- I was vigilant to any warning signs such as anxiousness or embarrassment
- If any of the participants showed signs of distress during an observation, audio recorders were to be turned off and the participant asked what support or space they might like at this point and offered time to recover. The participant would have been reminded that they were free to withdraw from the study at any time and asked if they wished to continue with the observation.
- Participants would have been offered further support via leaflets held by myself or would be signposted to relevant professionals for further advice where appropriate.
- If a serious concern had arisen during the observation (such as a potential overdose) I was ethically bound to intervene by the General Pharmaceutical Council's 'Standards of conduct, ethics and performance' [228] due to being a qualified pharmacist.
- If I had observed other safeguarding concerns such as clear signs that a participant was not coping (such as verbal or visual signs of abuse or mistreatment), I would refer to the appropriate services or contact my key contact for further advice.

Risk of harm to me

During each observation, there was the risk that a participant could become aggressive or abusive and physically or mentally hurt me. To reduce these risks a risk assessment was completed (Appendix 33) prior to observations commencing and a key contact (usually my supervisor) was made aware of where and when I was arriving and leaving each visit. Pre-prepared phrases such as 'I think I have left something in the car I need for this visit' were to be used if I needed to leave a potentially dangerous situation and call for further assistance.

5.3.9.2 *Respect for autonomy*

'Autonomy' means freedom from external constraint and this access to freedom and choice is rooted within our society. In order for PPs to engage with this study and for participants to be as open to me during the observations as possible, it was important that the autonomy of participants was respected. Some ways which I instigated this respect was by ensuring:

- Recruitment was voluntary
- Informed consent was present at each stage
- Appointments dates were set on the participant's terms

- Observations were on the participant's terms

5.3.9.3 *Justice*

Justice is ethically required in this study because everybody (including participants) must be treated fairly and without bias. Implementing justice involves treating equal cases equally and unequals unequally. Some ways that this was applied in this study were:

Access to information

To ensure that PPs provided their informed consent to the study, PPs needed to be fully aware of what the study involved. PPs were initially provided with the same basic level of information about the study and were informed that they had seven days to make their decision. However, I was aware and respectful of peoples' differences and if they needed a longer or shorter period of time to think about the study or needed more or less information before they made their decision, I would tailor the standard procedure to meet their needs without passing judgement.

Confidential information

It was important that all personal information (such as name, address and medication history) about each PP and participant remained confidential as ethically, people are entitled to their privacy and would expect for any information shared to only be used for a specified use within the research project. PPs were assured that any personal information shared during the project would remain confidential at all times, as otherwise this would have been a breach of PPs rights. Documents which stored personal information regarding the PPs and participants remained confidential in the following ways:

- **Paper-based documents** were stored in a secure locker within a secured room at the research sites. All information was destroyed two months after the study ended.
- **Personal information stored electronically** was transferred from paper records at the recruitment site to a password protected university laptop in a password protected file. This spreadsheet was regularly updated and maintained.
- **Photographs** did not show any personal data.
- **Dictaphones** always remained in the sight of me during observation commutes and I travelled directly home. Used Dictaphones had their files uploaded to a password protected file on a password protected laptop as soon as an observation had

finished. Once uploaded securely, the file was promptly deleted from the Dictaphone device.

- **Recordings** were transcribed and anonymised as soon as possible. Once transcribed and checked for accuracy, the computer files were permanently deleted from the laptop.

Anonymised Research data

Anonymity ensures that presented data cannot be traced back to the participants. This is important because if the data was identifiable this could have the potential to expose the participant to harmful health or social factors such as effects on their reputation amongst their community, on future employment and on their self-confidence. Anonymity was implemented in this study by applying generic 'C' (carer) and 'D' (PWD) on all transcripts and expanded accounts rather than using participant names. To further add anonymity, any mention of where they lived, or the names of their surgeries were blanked out and pseudonyms were used for the presentation of the data.

5.3.9.4 *Beneficence*

The Belmont report describes their 4th principle 'beneficence' to mean 'Maximise possible benefits and minimise possible harms' [227]. This means that the research should not cause harm to the participant, and that the researcher should ensure that the benefits to taking part are maximised and any potential risks minimised.

This study had limited scope for causing harm to participants but risks of emotional harm (such as embarrassment of talking about their dementia) were reduced by ensuring the participants were aware of what the study entailed in a comprehensive PIS, were reassured of the confidentiality and anonymity of any information disclosed and being aware and understanding that they were free to stop the study at any point and any disclosing of information during an observation was fully voluntary.

5.3.10 Data Analysis

Analysing data from focussed ethnographies requires the researcher to engage in an iterative, cyclic and self-reflective process, as preliminary interpretations are challenged, and data is continually revisited to plan for further data collection to generate new insights into the data [229]. The analysis of focussed ethnographic data is also characterised by the identification and classification of data, which then progresses to abstract generalisations and explanation of patterns [230].

An inductive approach was therefore used where 'the researcher begins with an area of study and allows the theory to emerge from the data' [231]. Thematic analysis is an analytical method which can be a robust and systematic framework for coding qualitative data and if often used in healthcare research. The coding system used in thematic analysis can be used to identify patterns (i.e. themes) across a dataset in relation to a research question [232].

Thematic analysis was therefore used as the primary analytical technique and was supported by computer software package NVivo 11®, which was used to identify codes and create subsequent categories and themes. The analysis followed six key phases [233] and Appendix 35 provides a work through example:

1. **Familiarising myself with the data** – I had deep engagement with the data by reading and re-reading the transcripts and observational accounts. At this stage, I also created and documented my early analytical observations
2. **Generating codes** – I systematically and thoroughly created meaningful labels attached to specific segments of the dataset. I used open, inclusive coding on both the transcriptions and the detailed expanded observation accounts. This meant that I labelled all segments of interest and relevance which related to the research question, the topic guide or provided context to a situation. My ongoing thoughts about the codes and the coding process were documented in my research diary which helped to process the emerging patterns in the data**.**
3. **Constructing themes** – Once the first couple of observations had been completed and codes generated, I was able to begin constructing my candidate themes. I examined the codes and combined, clustered or collapsed codes together into bigger or more meaningful patterns (candidate themes) using the research question as a guide. I did this alongside recording my thoughts and questions about the data and the emerging concepts and themes in my research diary.

   Codes continued to be generated after each observation and candidate themes were continually created, amended and evolved as the patterns became more apparent with increasing data. This process continued until no new themes emerged and data saturation was deemed to have occurred.

4. **Reviewing potential themes** – The candidate themes were further shaped, clarified or rejected by ensuring that the themes worked well in relation to the coded data, the dataset and the research question.
5. **Defining and naming themes** – I moved towards interpreting the themes orientation. This involved beginning to write the analyses and short theme definitions. Further shaping of the themes occurred and some themes were still able to be dropped or become sub-themes.
6. **Producing the report** - I moved from a 'purely' analytic point in the research process to coming back to the bigger picture of the overall project. This was aided by writing the results and findings reported later in this chapter.

5.3.11 Rigour

Rigour was important to consider during this qualitative study as it ensures that the processes used are transparent and consistent and thus enhances the quality of the findings. Rigour was ensured in this observational study by following Lincoln and Guba's four criteria [234, 235] which include Credibility, Transferability, Dependability and Confirmability.

Credibility refers to the value and believability of the findings [234] and can be achieved by conducting the research in a believable manner [236]. Strategies to meet this criterion during this study was by triangulating several data sources (expanded accounts, photographs and transcripts) and by peer debriefing with the periodic checking and review of written work by a supervisor.

Transferability refers to whether the findings can be transferred to another similar context or situation, while still preserving the meanings and inferences from the completed study [237]. To meet this criterion, expanded accounts included thick descriptions of the place of observation, the context of the conversations and details of what happened during the observation before and after the audio-recordings were written. These descriptions were enhanced by photographs taken during the observations and specific quotations from the transcriptions.

Dependability is similar to reliability in quantitative research and refers to whether the findings 'fit' the data from which they have derived [238, 239]. This can be gained through an auditing process and ensuring that the methodology is logical, traceable and clearly

documented by way of reflexivity [236, 239]. I continually used a research diary throughout this study to document each stage, my reflections from observations and my emerging themes. Additionally, the research diary, along with the participant recruitment and observation tracking sheets (Appendix 29.1 and 29.2) provided an audit trail of the research.

The final criteria for rigour, confirmability, refers to the neutrality and accuracy of the data and shows that the findings and interpretations are clearly linked to the data [239]. Strategies to incorporate this into the study were similar to that of dependability [236] with the use of reflexivity and an audit trail as described above

5.3.12 Training

As I had no previous experience in conducting observations, I gained experience in observing elderly patients talking about their medicines at their homes, using the observation guide, making jottings and writing expanded accounts by arranging time to shadow a medicines support technician prior to starting activities for this research study.

5.4 Results

5.4.1 Participants

Ten observations were carried out between October 2017 and January 2018 by which time, no new themes were emerging, and data saturation was reached.

The study included three PWD living independently and seven dyads. Including the informal carers there were seven males and ten females. Table 49 provides an overview of the ten observations with use of the pseudonyms. These pseudonyms are used throughout this chapter to provide continued anonymity of the participants.

Table 49. Participant(s) overview

Participant(s)	Living arrangements	Area overview	Medication overview		Contact with pharmacy
			PWD	Carer	
Mary	Lived alone with son in same village. Has 2 cats.	Lived in a bungalow in a fairly rural village outside of the city. Had good bus links to city and hospital.	Prescribed **7** medicines. Cat also prescribed a thyroid medicine.		Little. Sometimes collected medicines when able.
Penny	Lived alone	Lived in a new-build bungalow <15 years old in rural village outside city. Lived off a quiet road which was only busy during commuting times.	Prescribed **6** medicines. Used a dossette box.		None.
Bob and Jane	Lived together as a couple. Jane had dementia. Had 2 dogs.	Lived in a bungalow down a narrow, unkept road in an isolated part of the county where most homes were holiday homes. No facilities or transport links.	Prescribed **2** medicines **PLUS** a trial medicine for dementia.	Prescribed **3** medicines	Regular contact with pharmacy by both together.
David and Janet	Lived together as a couple. David had dementia. Had a cat.	Lived in a bungalow in a quiet cul-de-sac in a popular tourist village on the outskirts of the city with public transport links and many facilities nearby.	Prescribed **8+** medicines including various creams used irregularly	Unknown	Little contact, mostly by Janet.
Sylvia and Debby	Daughter (Debby) lived with mother (Sylvia) who had dementia. Debby had her own living space but they shared the kitchen.	Lived in a detached house situated on a quiet road off popular tourist village on the outskirts of the city with public transport links and many facilities nearby.	Prescribed **3** medicines. Used a dossette box. Occasional use of non-prescribed medicines such as paracetamol.	Unknown.	No contact by Sylvia. Some contact by Debby on Sylvia's behalf.
George and Sally	Husband and wife where George had dementia.	Lived in a bungalow within a town which had good transport links and walking access to many services and facilities.	Prescribed **9** medicines.	Unknown but aware some prescribed.	Little contact by George, regular contact by Sally
Harry	Lived alone.	Lived in an end of terrace, Victorian style house in a town with access to public transport and facilities	Prescribed **11+** medicines including some medicines which were used irregularly.		Regular contact.
Edward and Jenny	Husband and wife where Edward had dementia	Lived in a terraced, Victorian style house in a town with access to public transport and facilities	Prescribed **4** medicines. Used **2** additional vitamins. Pill box used.	Recently stopped.	Regular contact by both together.
Jack and Louise	Husband and wife where Jack had dementia.	Lived in a multi-storey apartment within a medium sized stately home in a town with access to public transport and many facilities	Recently prescribed first ever medicine (Memantine).	Prescribed **5** medicines.	No contact by Jack. Regular contact by Louise.
Peter and Amy	Husband and wife where Peter had dementia and Amy was notably younger than Peter. Had a cat.	Lived in an apartment within a council/ex-council housing area of a town with good access to public transport and facilities.	Prescribed **2** medicines. Only 1 was taken daily.	Prescribed **1** medicine.	Regular contact by both.

5.4.2 Themes

As each transcript and expanded account were coded and discussed in the research diary (see Appendix 35 for further information), five themes were produced that characterised patterns in ways the people observed managed their medicines whilst living with dementia.

1. **Daily routines**: How the daily routines of both PWD and carers framed ways that they managed their medicines.
2. **Support from family and objects:** How PWD had support from both family members and objects and how these may or may not have aided their everyday lives and the management of their medicines.
3. **Managing multiple medicines:** How both PWD and carers engaged with multiple medicines and their experiences associated with them.
4. **Living with one or more health condition besides memory loss in dementia:** How other symptoms of the dementia other than memory loss or other health conditions impacted the lives of both the PWD and the carer and in turn how this affected ways they manage their medicines.
5. **Engaging with healthcare providers:** How healthcare providers such as GPs and pharmacies influence how PWD and their carers manage their medicines.

In the following pages, I provide examples from the expanded accounts and transcripts, along with photographs to exemplify how these themes provide understandings of how people affected by dementia manage their medicines within the community.

I have chosen examples which best represent how and why people affected by dementia manage their medicines in the ways that they did, and which reflect the wide range of data that was gathered.

Theme 1

Daily routines: How the daily routines of both PWD and carers framed ways that they managed their medicines.

Most observations featured peoples' use of routines to order their everyday lives where the participant takes part in activities which are part of their day-to-day lives.

Mary, Penny, Syvlia and Debby, George and Sally, Harry, Edward and Jenny, Jack and Louise and Peter and Amy were all observed to have routines where the participant visited the same area of their house each day, for instance, going to the kitchen when they woke up to make a cup of tea or to pour a glass of water. These participants were also observed to have incorporated their medicines or other objects such as a diary into these routines by ensuring they were placed plainly in sight in an area which they knew they would visit as part of their routine.

David and Janet only kept some medicines (inhalers) in areas which were incorporated into their daily routine (next to David's bed and chair where he spent most of his time) whilst the remaining medicines were stored out of sight for Janet to access when needed.

Bob and Jane's daily routine consisted of an out of house activity (walking the dogs) in the morning, and then having a hot drink followed by Bob giving Jane her tablets which were stored in a kitchen cupboard near the kettle.

The observations relating to routine from Penny, Jack and Louise and Sylvia and Debby are described in detail below as these give examples of how both PWD and carers have incorporated medicines into daily routines.

Penny – *Penny's medicine routine*

Whilst I was at Penny's home during the morning and Penny gave me a tour of the bungalow, I spotted a small plastic pot with coloured tablets in it along with a glass of orange juice on the bedside table to the left of Penny's bed (See Figure 12). I asked Penny if these tablets were her night medicines and Penny replied 'this is how I do every morning. When I get up, that's the first thing I do, is to put my tablets and my orange juice [in the pot and bring them into the bedroom]. And then I take them again [as in every night] when I go to bed. And then the next morning before I do anything else, I bring them [the pot and the cup back into the kitchen], and put them [put the new tablets in]'.

Penny only takes medicines once a day, in the evening and this observation showed how the routine morning activity of waking up, taking the empty medicine pot to the kitchen and making a drink, refilling the pot and glass and placing back by the bedside table every morning) and then having the medicines placed somewhere as a visual reminder (by the bed when Penny gets into bed) were important mechanisms to have in place to help her to remember to take her medicines every day.

Figure 12. Penny's tablets and orange juice ready by the bed to be taken later on in the evening

Jack and Louise – *Carer's routine used to manage Jack's medicines*

Another example, this time where the carer had established a routine in order to manage both their own medicines and also those of the PWD was in the case of Louise and Jack. Louise previously had an established routine for her own medicines which had to be taken twice a day and this observation showed me how Louise had recently had to adapt her routine to also accommodate Jack's newly (and only) prescribed once a day medicine for dementia.

Near the beginning of this observation whilst we were sitting around the dining table, Louise suggested 'well let me take you, show me what how what I do how to keep our [medicines]' to which I enthusiastically agreed. Louise stood up and told me to follow her. Jack and I followed Louise through another door into a hallway and up a carpeted staircase which seemed to have 2 separate 90 degree turns in it. Whilst walking up the stairs, Jack told me how he hadn't been on any medicines until this new medicine. Jack and I continued to follow Louise from the stairs into their bedroom and around the bed. Here, Louise showed me how she keeps a small pink makeup/ toiletry bag which she called a pochette under her pillow along with her pyjamas. Inside the bag were loose blisters of various

medicines of hers and also Peter's memantine. Louise explained to me that she keeps them in a bag under her pillow because then when she goes up to bed she finds a visual reminder for her to take her evening medicines. When she has taken her evening medicines she then places it on a side-table to the left of the bedroom (behind where I was standing) which is then a visual reminder in the morning for her to take her morning medicines (see Figure 13 for a bedroom layout above). Once the morning medicines have been taken, she then placed the evening meal medicines (one metformin for Louise and the memantine for Peter) into a pill box (Figure 14) in preparation for when they have their evening meal.

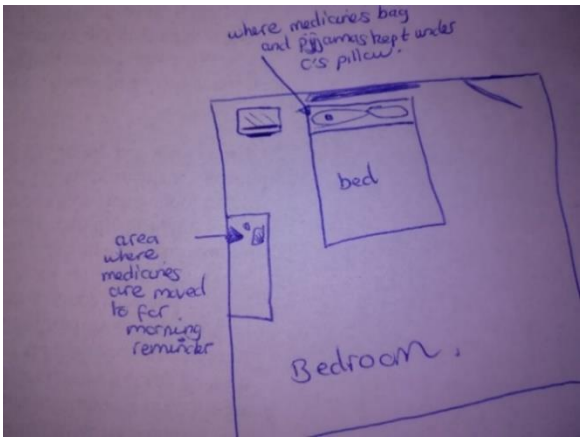

Figure 13. Louise and Jack's bedroom layout

Figure 14. Louise's pill holder

This observation showed how sometimes people will make multiple step changes in a daily routine to fit ways of managing medicines around their practices and preferences. In this case, Louise's usual bedtime routine was to take her pyjamas out from under her bed pillow, put the pyjamas on and go to bed and her usual morning routine was to wake up, make the bed and place the pyjamas back under her pillow and get dressed using items from the bedroom sideboard before going downstairs for the day.

This observation saw how this daily routine was adapted to incorporate both her and Jack's medicines. Louise placed the evening medicines on her pyjamas under pillow in the morning when she woke up so that when she went up to bed and got undressed, she would see the evening medicines as a visual reminder and know that she needed to take them. She would then place her morning and evening meal medicines on the sideboard before she went to sleep so that when she got dressed in the morning the medicines she needed to remember to take during the day were in her line of sight. Louise would then be reminded to take her morning medicines and then place her evening meal medicine and

Jack's medicine into the silver box, take it downstairs with her and place it somewhere in plain site (often the dining table) as a reminder for the evening meal medicines to be taken.

Sylvia and Debby – *Sylvia's daily routine*

A final example of how medicines were observed to have been incorporated into the daily routine of a PWD was in the case of Sylvia and Debby. Sylvia's usual morning activity was to wake up, go to the kitchen, enter the larder where the cereal is kept, pour cereal into a bowl, sit down at the table and eat breakfast. Below describes Sylvia's new routine which incorporates her medicines.

During another early morning observation, I observed some paracetamol as well as Tesco cold and flu remedies on a kitchen surface to her left. Answering a query about why they were stored there, Debby explained to me that the other medicines (regular daily medicines) were stored in the larder in the kitchen before being taken out and put on the side by the sink, when Sylvia got out her cereal every morning. I looked over to where Debby was now standing and there I saw a translucent dossette box placed out on the side with a box of memantine hidden behind a kitchen roll by the wall on the same counter. I later asked Debby and Sylvia if she could have a look in the larder where they had mentioned the box was usually kept. I opened the larder door adjacent to where the tablets were (Figure 15) and Debby walked over to show me where the tablets usually went but also how they had to be moved to a different (but equally visible shelf) over Christmas due to all the Christmas chocolate she had acquired.

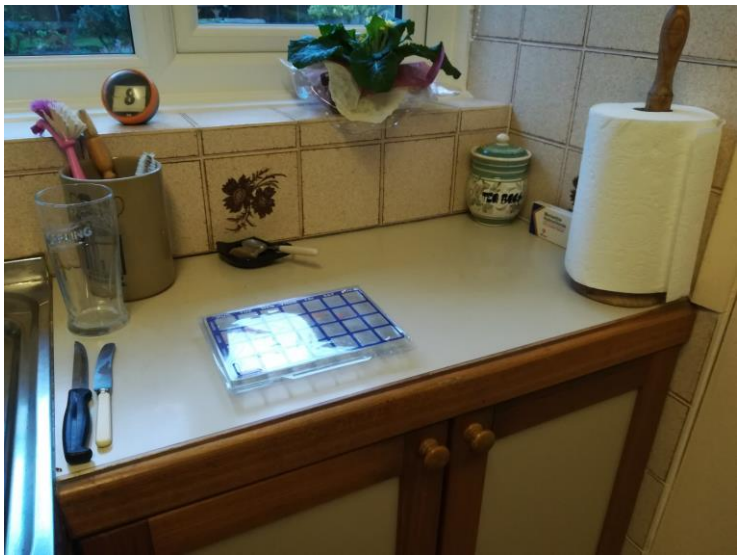

Figure 15. Sylvia's medicines out of the larder in preparation of being administered

In Figure 15, a separate box of memantine was visible by the kitchen roll which Sylvia had only recently been prescribed and was to be taken at night, whereas all her other medicines were in the morning which was why her current routine of storing the medicines with her cereal had worked effectively up till now. However, Debby later described in this observation, how she needed to find a new routine to aid the remembering (for both of them) of an evening medicine after she realised that she had recently forgotten to administer the new medicine.

"Which actually, of course, yesterday we had lunch at lunchtime, I didn't give you any night medication. That's the problem I've got to remember. 'Cause normally I give it to you with dinner… No, Sunday's is still here. So that's my fault… we'll have to come to some sort of system whereby I remember that it's there … I need something to trigger me to… give it to you" *(Debby. Carer to PWD)*

This final observation showed both how routines could be useful to both PWD and their carers, but also what could happen when medicines change and how routines need to be constantly made visible and reviewed for ensuring medicines could be successfully managed in the long-term.

In summary, most, if not all of the participants were observed to have routines throughout the day with largely the morning routine activities being observed. In many cases it was the morning routines which incorporated the participant's medicines which had been purposefully placed in strategic places where the participants knew they would see the medicines as they carried out their usual routines. This enabled the participants to remain more independent with their medicines by helping them to remember which and when medicines needed to be taken and helped ensure that the medicines were taken safely.

Theme 2

Support from family and objects: How PWD had support from both family members and objects and how these may or may not have aided their everyday lives and the management of their medicines.

The observations drew to attention that all of the participants living with dementia relied on some form of support in order to manage their medicines within the community. The support of physical objects were observed in 7 of the observations which included dossette boxes, diaries, calendars, reminder notes and electronic emergency buzzers. The support of family, friends and neighbours were also described during 9 of the observations and amongst those that lived with their informal carer, the observations made it very clear that these PWD relied heavily on their carer to take control of most aspects of their medicines with particular emphasis on the remembering of and administration of the medicines.

Below, Mary and Penny's supportive mechanisms are described in detail to show how a range of support is being used to meet the needs of the individual. David and Janet's observation of support has also been described because it portrays how David has increasingly become more reliant on Janet to manage his medicines for him as the dementia has progressed.

Mary - *Adapted diary and notepad to make reminders*

During my visit with Mary, I asked if she had come up with any ways to adapt. Mary replied that she had something to show me that she thought would make me smile. Mary picked up a small book from the kitchen table where I was sat and opened it to show me the inside pages. There were spaces for each day of the year which Mary explained she used to keep a note of when she woke up/took her first medicines and when she took her night time tablets and went to sleep (Figure 16). She also explained how the book was also used to write any other appointments that were coming up to help her remember. I showed great interest in this and Mary told her how she would have been happy to buy it [in the future as this one came free with a magazine] and how it was a handy jotter and helped her remember day to day things such as the day or the date.

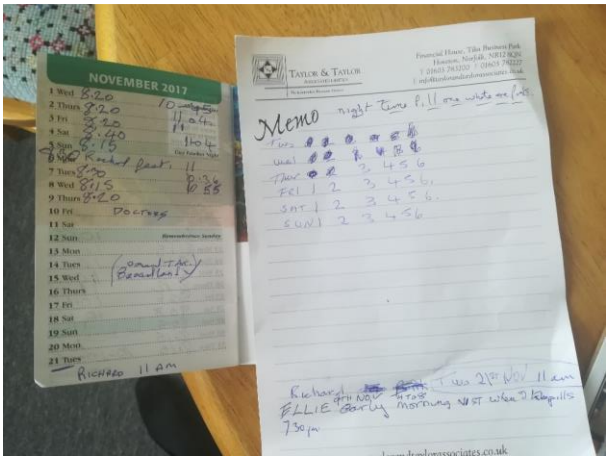

Figure 16. Mary's adapted objects to help support her memory

I then asked Mary if she had anything else to help her keep track of her medicines. Mary showed me a piece of A5 paper (Figure 16) which she used every week to help remember when the tablets were taken and then crossed the numbers off each time they were taken. She used the bottom of the page to write any other appointments coming up that week (such as my visit). Mary told me how she also used the back of the paper as her cat was 'naughty and won't take his medicines so I write it down what he do'.

This example highlighted how for those that live alone with dementia, using objects and practices to remind them and to record day-to-day tasks may be used to help them manage their medicines such as when medicines are to be taken. Mary is aware of her dementia and some of her difficulties such as remembering when medicines have been taken and has therefore found a documentary way which works for her to track and remind herself when medicines have been taken and how many are left to take.

Penny – *Whiteboard, calendar, reminder notes, dossette box and emergency button designed to support everyday life*

Penny had several objects specially designed to help support her with her daily life. During the tour of her bungalow, Penny led me straight through the kitchen into the utility room. I spotted a white board on the fridge which had some phone numbers and writing on. I asked Penny if this was one of her reminding methods. Penny agreed but did not say very much about it except 'that's telling me about the washing machine and erm…'. Penny and I then moved back into the large white kitchen towards the counter surfaces where I was instantly drawn to a whole line of paperwork (Figure 17) spread out across work surface in a long line such as a diary opened on this week, bits of paper with reminder notes on such as 'Ellie 9.30', and a dossette box (Figure 18) with a history of many dossette box sheets

piled together behind the opened lid and a reminder note on the box saying ‘bedtime only’. Penny went on to tell me how one day she took the wrong tablets and how she pressed her button on her neck alarm she wears (at this, she points to the circular red button against a black background which hung around her neck by some string). She told me how she had had the button for years and how she hung it on the chest of drawers next to the bed each night and that was how she remembered to put it on each day.

Figure 17. Penny's other objects supporting daily life

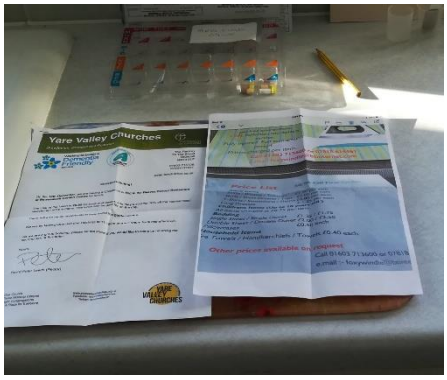

Figure 18. Penny's dossette box

Penny showed me how, like with Mary, a PWD and living alone may need further assistance to help remember certain aspects of her day-to-day life such as upcoming trips away and her medicines. Similar to Mary, physical objects such as the calendar and diary were visually on display where Penny could record events which she needed prompting for as she was aware of her dementia causing her memory problems and confusion. Unlike Mary, Penny also had the support of a dossette box for her medicines which helped Penny with the storing, organisation and taking of her medicines as she did not have to think about what time of day the different medicines were to be taken (as they were all placed in the bedtime slot) or where to store a number of tablet boxes (as were already popped out for her into the specific time slots).

The electric button Penny wore also shows how technology can be used to enhance the lives of PWD, especially of those who live alone and can support someone with dementia to be able to live independently with confidence and reassurance that if something did go wrong (such as a fall), the support of a HCP is just a button press away. In this case this was adapted to take action after a medication overdose.

Penny related an anecdote during her observation where her sister helped support her with running her daily life:

"My sister came over yesterday, she always come do my hair once a week." *(Penny. PWD living alone)*

This kind of wider supportive network could also be seen with Mary whose son helped with ensuring the medicines of the PWD living alone could be collected on time.

"Harry [son] I said, I can't collect them blimmin' pills till 4 o clock, so I said, will you nip in and get them for me? So he say, 'yeah of course I will mum, it won't take me a minute'". *(Mary. PWD living alone)*

These anecdotes show how family can help support PWD who live alone in a number of ways and that this could also be applied to collecting medicines. For Mary, she was unable to collect her medicines but her son seemed happy to collect them for her reinforcing that it wasn't a problem by emphasising that it would not take him long. This ensured that Mary was able to keep taking her medicines without disrupting her routine which could otherwise have led to unnecessary emotional or health-related harm to Mary.

Penny had her sister visit her every week to do her hair for her. This weekly meeting provided Penny not only with physical support of having her hair done, but also emotional support. This weekly meeting provided Penny with an opportunity to see her sister and take part in a social experience which could otherwise have been difficult for her to do.

The PWD who lived with informal carers (usually their spouse) tended to rely less on using a combination of supportive objects such as diaries and reminder notes and more on their carer when it came to the management of their medicines. The carers were often observed to be the person who ordered, collected, organised and prepared the PWDs medicines with varying degrees of input from the PWD.

David and Janet – *Janet (carer) in control of medicine organisation and administration*

When the time came during this observation for David to take his daily afternoon medicines, Janet showed me what usually happens. I joined Janet in the bedroom (after initially forgetting the audiorecorder) and David remained in his seat in the lounge where the observation had been taking place until now. Janet showed me how David's many medicines were stored under her single bed and in the drawer of the bedside table between the two beds. Janet explained how the medicines in the drawer were the ones that David was currently taking regularly (Figure 19). Janet took me through the medicines as she popped them out one-by-one and also showed me about 6 weekly medicine mini plastic pill organisers which she explained were not used anymore but were used prior to

the dementia and when David could manage his own medicines. Janet explained that David did not really know what he took any more, nor when and that he even needed reminders to take the inhaler in the morning and night that had been placed right next to his bed.

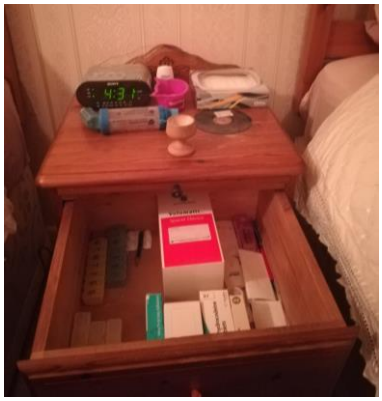

Figure 19. David's regular medicines and egg cup used for Janet to transfer dispensed medicines to David

This example shows how the carer is aware of David's limitations since the dementia was diagnosed and had accepted that she needed to provide further support to him by taking control of his ordering, storing and administration of tablets.

Overall PWD used a range of support which ranged from physical objects such as diaries and reminder notes to the support of their carers, family and friends to help them with their everyday lives. These support mechanisms were seen to be key features for helping PWD to manage their medicines in many ways from collecting the medicines, storing and organising the medicines, remembering their medicines and giving the medicines to the PWD to take.

Theme 3

Managing multiple medicines: How both PWD and carers engaged with multiple medicines and their experiences associated with them.

Nine of the ten PWD observed were prescribed more than one medicine, with some, such as Mary and Harry) requiring them to be taken at various times of the day. During the observations, it became clear that PWD and their carers were not only needing to order, collect, organise and remember to take one medicine for the dementia but that often the carers, such as Louise and Amy also had their own medicines to manage too.

Difficulties with managing multiple medicines were observed in such cases as Sylvia and Debby who were trying to incorporate the new dementia medicine into their already established routine, Mary who had similar looking tablets and Jane who had experienced side effects with new medicines.

Some participants however did describe the benefits of their medicines such as Penny who felt that her memory and ability to hold conversations had improved.

Some observations where these different experiences were seen or described in detail are shown below under the headings of: Multiple medicines, problems faced regarding medicines and the benefits of medicines.

Multiple medicines

Six of the PWD were prescribed between 6-10 medicines, one participant (Harry) was prescribed more than ten and one participant (Jack) was prescribed only one tablet. Not all of the carers went into detail about their own medicines but the 4 who did were prescribed less than five.

Harry – *Prescribed and ordering a large number of medicines*

During my visit to Harry, he mentioned that he took 10 tablets in the morning and so I asked him if he could show me where they were. Harry said ‘Yes! Come on!’, put his pipe down on the coffee table in front of where he was sitting in the lounge and walked out into the hallway and into the kitchen. I followed Harry into the kitchen and he said ‘they’re all here’. On the kitchen surface to the right of the doorway were several tablet boxes (see Chapter 5. Observation study

Figure 21) and a small diary with blood glucose numbers written on it. Harry then added that ‘and there’s also some, and there’s also some in the in the in the cupboard in the erm, in the toilet first on the right there’ whilst pointing to a room straight ahead. ‘Those [in the toilet] were the spare ones’.

Later on in the observation, Harry led me upstairs to show me some more of his medicines (including his new dementia tablet) which he kept on top of a chest of drawers in his bedroom (Figure 20) and said ‘and here’s the stuff I take’.

After hearing about Harry’s bedroom tablets and his routine, Harry led me downstairs again, where I asked if she could have a look at the medicines Harry had mentioned he kept in a bathroom. Harry directed me to a large cupboard in his upstairs bathroom which had 3 levels of shelves containing an assortment of creams, prescribed and non-prescribed medicines and what looked like an unused catheter which were all arranged neatly (Figure 22).

Harry had organised his many medicines by finding different storage areas for each medicine around his home. The ones he knew he needed to take regularly, he had placed in areas of the home where they would be seen during different parts of his routine (such as the kitchen and bedroom chest of drawers). The spare medicines and irregularly used medicines and creams had been placed in a cupboard in the upstairs bathroom. This meant that Harry still saw the medicines whenever he went into the bathroom and so would be consistently reminded of what medicines he had and where they were stored, but were not taking up valuable space in the kitchen or bedroom.

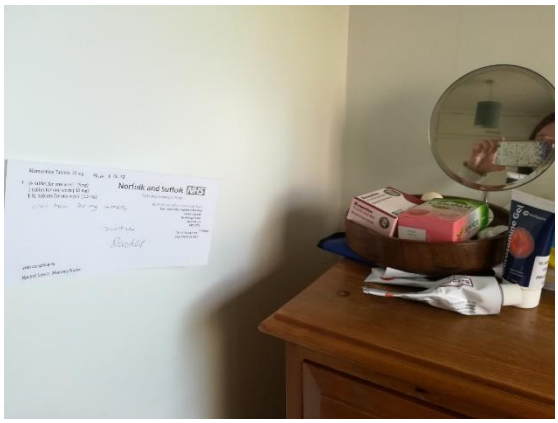

Figure 20. Harry's bedroom medicines

Figure 21. Harry's kitchen medicines

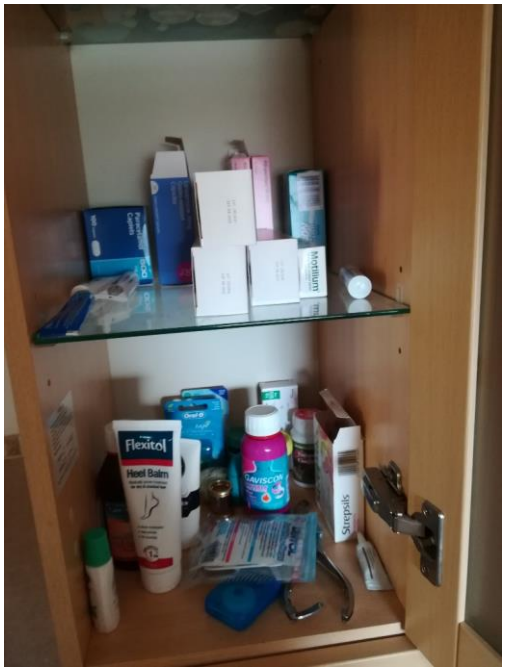

Figure 22. Harry's bathroom medicines

Problems faced regarding multiple medicines

Four of these observations revealed issues with either medication aides or the medicines themselves. Sylvia (PWD) found it difficult to open the cellophane lids on her dossette box, Jenny (carer) did not find the Rivastigmine patches placement sheet provided by the manufacturers user-friendly and Mary found some of the colours and shapes of her many tablets to be confusing. Another problem faced by roughly 50% of the participants was side effects such as hallucinations, bad dreams and diarrhoea to their new dementia medicines.

Mary – *Visually confusing tablets*

When it was time for Mary to take some of her medicines, she opened up the Levothyroxine 50mcg tablet box and, with some difficulty, popped the tablet out of the blister foil. Mary showed me the tablet and said 'do you know what, you could muddle that up with that… sleep… that pill I take.' I had a look at the small white tablet and from experience knew it did look like the sleeping tablet zopiclone and nodded in agreement to Mary and said 'yes!'. Mary then opened the packaging of the 25mcg levothyroxine tablet (again with a bit of difficulty) and showed me both tablets together and said 'look! That's 50. That's 25. And that's huge! How weird!'. I noticed that Mary was indeed correct, the 25mcg tablet was almost double the size of the 50mcg tablet. Mary continues by saying how 'it'd be very easy to muddle them two up wouldn't it'.

This example shows how similar some medicines can look even if they were for very different indications and also how the size of a tablet may not bear any relation to its strength. Mary highlights how confusing this can be for some people, particularly PWD and how easy it may be for someone to make a mistake such as taking the wrong tablets at the wrong time or taking too many of one tablet and not enough of another tablet.

Bob and Jane – *side effects of multiple medicines*

Jane was taking part in a new dementia medicine trial and after Bob showed me the trial medicine and administering Jane's tablets, I asked whilst still sitting on the floor looking at the trial medicine box which medicine came first out of the trial medicine and the dementia medicine (memantine). Bob, who was sitting on the sofa with one of the dogs next to him replied that 'this [memantine] is the third one of these [dementia medicines] that we've been on… cause they've, they've not suited her. Yes so. We're just gradually increasing the dose on this one… yeah, the first one we were on, you had really bad diarrhoea and stomach problems.' Jane then added 'that was terrible yeah'. Bob further elaborated 'and then, the second one erm, started off on the low dose and then once we got to the stronger dose, you were getting really bad er… visual nightmares.' 'Yes!' Jane replied. 'Like flashing in my eyes and things.'

Jane was one of several participants who had experienced side effects like this with a dementia medicine. This experience described by Bob and Jane shows the impact these side effects can have and how it led to the medicine being changed several times. The repeated changing of medicines could be confusing for PWD as their reduced cognition could make it difficult for them to understand why the medicine has changed name, shape, colour and packaging and may be unsure whether they should take the medicine. This could therefore lead to a PWD either not taking the medicine as prescribed or not taking the medicine at all.

Benefits of medicines when multiple medicines were prescribed

Some participants spoke about how they had felt that their medicines were benefitting them and one good example of this was with Penny who was prescribed several medicines and had recently experienced side effects from her new dementia medicine.

Penny – *Symptoms improvement after initial side effects*

When Penny was showing me her dossette box of medicines in the kitchen, I asked Penny if she had experienced any problems with them. Penny had gone on to explain how she had

experienced terrifying nightmares including one which involved her sister being a baby and being stolen. Penny explained how she had to 'get up and go through the house to see if there was any sins that I'd got a baby to look after… it's so frightening it really is'.

However, later on in the observation when Penny and I were sitting in the lounge discussing how long term memories were engrained Penny refers back to the nightmares and how she is glad she continued taking the tablet as she has since noticed an improvement in her memory and concentration.

"But I've been better since I've been on that tablet I mean I put up with nightmares, they were horrible. But I thought… if I give those up… you know… I feel personally… that I'm not as bad as I was. I can… remember most things. I mean I don't go into the kitchen to get something and forgot what I go for. You know, I… which I did before. I could get up and go to the kitchen and think, well what on earth have I come in here for. But I don't anymore, I. You know, whether that's the tablets or whether that's, you know… what I don't know but erm… and I would have found it probably difficult to erm… hold a conversation… before… which now… I probably gabble on." *(Penny. PWD who lives alone)*

This example shows how sometimes people can find out it is worth persevering with new medicines as unpleasant side effects can sometime wear off to leave potential benefits to the patient.

Overall, the varied experiences described in this theme show how PWD manage the organising, storing and taking of multiple medicines and how sometimes they have had to manage the side effects of their medicines which in some cases led to the medicines being changed multiple times and in other cases, subsided to leave the benefits of the medicine.

Theme 4

Living with one or more health condition besides memory loss in dementia: How other symptoms of the dementia other than memory loss or other health conditions impacted the lives of both the PWD and the carer and in turn how this affected ways they manage their medicines.

Many of the participants were observed to have additional health conditions which impacted their everyday lives. Notably, Mary, David and Peter had difficulties with hearing and Penny, David, Sylvia and George had difficulties walking. Furthermore, symptoms of the dementia such as difficulties remembering words, holding conversations and describing past events were observed in participants such as Peter, Jane and Penny. These difficulties faced by the participants were seen to impact how medicines were managed as R noted that those who had difficulties walking tended to have medicines delivered and not visit their pharmacy in person and those that had difficulties hearing consequently found it difficult to speak to HCPs when needed.

Some of the carers such as Jenny and Sally also had health conditions to contend with such as recurring cancer or arthritis in their fingers which also affected the daily lives of the dyads and consequently, how they went on to manage their medicines.

How dementia and other health conditions of both the PWD and carer were observed to impact day-to-day life are described in the examples below.

Multiple dementia symptoms which affect PWDs day-to-day lives

Alongside the memory problems which may have been expected in dementia (such as memory loss and confusion), other problems some of the PWD faced concerned difficulties with organising and accomplishing household tasks such as making a cup of tea or using the oven, finding the right words, finishing sentences and concentration.

Amy and Peter – *Dementia symptoms affecting simple tasks and conversations*

Early on in the observation Peter was retailing an anecdote to me about how he sometimes made silly mistakes such as when he got muddled with making a cup of tea.

"I make silly mistakes. I really do. Erm… there's one I did wrong, I can't remember now. That that is the wor- horrid old thing. Er, when I make me cup of tea… I, I've put the cup on the table. Not on the table. Out in the kitchen. Erm… put… oh god, the tea bag in the cup… and erm… boiling water…and

er, got the tea bag out. And put into a thing. Out the way. Erm, went to the fridge to get the, milk. Put the milk in. and erm, that was that. Fine. I, know, went into the other room… and sat in there… quite a few hours I think and thought I would have another cup of tea…. Went back. And erm… put the, er, the erm… cup on the… thing outside out the kitchen, put the hot water in the bag and that took the bag out. Stirred it. Went to the fridge to get to get the milk. No milk… I'd lost it… I didn't know where I'd put it or anything. She come home from work and found it. Under the sink." *(Peter. PWD with a carer)*

This extract not only describes the difficulties PWD can have with simple tasks such as making a cup of tea, but also shows how difficult it can be for a PWD to speak to people and make conversation as the story has a lot of pauses, 'erms', some mistakes with words chosen and told in a broken up fashion. The difficulties with finding the correct words was then shown again later on when Peter was telling R about his experiences with his pharmacy he said 'yeah. oh 'cause, I, help and loads of other people in this town, who, you know, help I'll go to the dentist for em. Not dentist. What do I mean <chuckle> erm, Boots <chuckle> why am I thinking dentist?! Stupid idiot!'

These difficulties with completing tasks and the difficulties with relaying a story in conversation shown here mean that other simple tasks such as taking out and placing a new medicine patch onto the body, or simple conversations such as speaking to a GP and trying to convey the problem that they have come to see the doctor about can also difficult which has the potential to lead to reduced medicines management.

Other morbidities of PWD which affect their day-to-day lives

Two PWD had severe hearing problems, and arthritis and other muscular or joint problems were also evident in some observations (such as difficulties opening tablet blisters and Weetabix boxes). Issues faced by PWD regarding these morbidities were either noticeable during the observations or were described anecdotally by the PWD.

David and Janet – *Day-to-day life and managing medicines affected by difficulties hearing and walking*

At the beginning of this observation I took a seat adjacent to David with a distance of about one-two metres. Once the recorder was on for this observation, it became quickly apparent that due to where I was sitting, David could not hear her as he said 'sorry, I can't hear you'. I moved her chair nearer towards David and asked if he 'could hear me now' using a louder voice. Janet then explains how David doesn't answer the phone because of his hearing problem.

Later in the observation Janet asked me if I would like a cup of tea or something. I replied 'I'm fine thank you' but David replied 'yes I would thanks. That would be a good idea!'. I then observed David turn his swivel chair towards a tray which was sitting next to him on a stool which held a tea maker, cups, tea bags, milk sachets and a pot to put the tea bag in afterwards. David switched on the teamaker and I observed him make himself a cup of tea from where he was sitting. Janet went on to tell me how David wasn't very stable walking after breaking his hip from falling onto a concrete floor which is why there was a teamaker in the lounge for him to use. I asked David if he used a stick and Janet said that he had 2 sticks. David added how he liked his main stick being adjustable and having a good grip on the top. I then spotted the stick sat next to David and saw the grip that David was talking about. There were ridges on it for the fingers which David explained made it easier to hold.

This example shows firstly how even in day-to-day conversations, hearing difficulties can cause problems as David was unable to answer the phone or hear other people unless they were speaking very close to him. This meant that ordering medicines and making HCP appointments (both often over the phone) or having HCP telephone consultations were difficult for David. In addition David found it very difficult to walk around the home to even make himself a cup of tea. This meant that David also found it difficult to leave the house to even visit his local surgery or pharmacy which then impacted how they order and collect their medicines (Janet orders the medicines and David had his delivered).

Carer morbidities which affect their day-to-day lives

Some of the carers were also observed to have morbidities which can impact their everyday lives.

Edward and Jenny – *Jenny (carer) living with cancer as well as caring for a person with dementia*

During the recruitment meeting and subsequent phone calls arranging this observation, I had previously learnt that Jenny had ovarian cancer and was due to go into hospital imminently for an operation. When Jenny spoke about how 'we muddle along' during the observation taking place in their kitchen, Jenny tells me more about her experiences with cancer.

"I've been on letrozole. Since erm, I had surgery, 2 years ago and then, I've had, this is my third lot of surgery so… the first time it didn't work, they couldn't remove it. So had chemotherapy and that shrank the tumours… 2 years ago from now I had more surgery and they were able to move, remove lots... And so then I had more chemo. And then the oncologist put me on letrozole... He said stop it a

week before the operation so I've stopped that. And, then, apparently, I've got, another surgery, and then I've got 6 lots of chemo, and then, go back on the letrozole after that. So. The the surgeon, consultant surgeon, is not convinced that letrozole does anything but the oncologist feels it's worth a try so I, I just do as I'm told <Janet laughs> So yeeah. We'll see how it goes…fingers crossed I get through chemo very easily. I have about… what about 2 or 3 days after, I've had it, erm… I feel a bit light headed, I wouldn't drive. I feel a bit lightheaded and I don't do very much. But I haven't felt sick, I haven't felt… feel tired, but that's that's it really, I just feel fine. I've been extraordinarily lucky really, very fortunate." *(Jenny. Carer to PWD)*

Jenny later explained how before she goes into hospital she would 'fill them up [Edward's weekly dossette box] before I go in' and whilst she is to be in hospital she faced further problems.

"And D would be perfectly happy cooking for himself. But now of course, he can't do that [due to dementia] which is one of the problems for when I'm in hospital… <son> will be here until… probably the Wednesday but he'll have to get back to work, erm, got lots of friends who are coming in with food…I mean, church people have been absolutely fantastic haven't they? Really, really. Kind and… offers of, of been driven into Norwich, into the hospital. So when <son> goes home, erm, we'll have a little rota up of people to take, D in to see me." (Jenny. Carer to PWD)

Janet's own extended treatment meant she had needed to find other help for Edward which involved someone helping to remind Edward about his daily medicines, cooking and other day-to-day tasks.

This example shows how carers may be experiencing their own health problems whilst also trying to care for PWD. Jenny was fighting her own battle with cancer and had been for several years, yet was also needing to find a way to continue to support her husband with day-to-day tasks (including medicines management) whilst she was in hospital.

In summary, the experiences within this theme have shown how the day-to-day lives are not only affected by symptoms of their dementia, but also by other health conditions or the health conditions of their carers. Consequently, living with these conditions or the symptoms of dementia have shaped how their medicines are managed such as how medicines are ordered or collected or taken.

Theme 5

Engaging with healthcare providers: How healthcare providers such as GPs and pharmacies influence how PWD and their carers manage their medicines.

Healthcare providers are responsible for diagnosing and reviewing medical conditions, prescribing and reviewing medicines and dispensing and providing the medicines to the patient. Participants described during the general conversations had within the observations mixed accounts of their use and experience of healthcare providers which may influence how they consequently managed their medicines.

Experiences described by the participants of how healthcare providers influenced their medicines management included issues of communication and contact that shaped the accessibility of both the healthcare providers the medicines.

Mary, Penny, David and Syvlia had their medicines delivered to ensure that they had access to their medicines whilst Peter, Louise, Jenny, Harry and Bob had a pharmacy either within walking or driving distance and were mobile enough to collect their medicines in person. Additionally, Debby and Sylvia were very complimentary about their GP surgery and found it very accessible and were happy to use it whereas Bob and Jane described how difficult it was to get an appointment at their surgery and how there were no easily accessible healthcare providers 'out of hours' which meant that they did not always see the required HCP when they needed it.

*Experiences relating to access to **healthcare providers***

There were many experiences participants described during the observations in relation to their social and physical access to healthcare providers (notably surgeries and pharmacies).

Jenny (carer) explained to me during their observation how they 'go to the practice nurse first, they're very user friendly the practice nurses there' whilst Debby (carer) described how 'GP surgery is great because it's just down the road, parking is easy and it's flat.' Sylvia, Debby's daughter added to this how 'that's right, there's loads of chairs'.

The option to see a nurse rather than a doctor and the ease of accessing the surgery itself were seen as great benefit by these participants. These factors mean that the PWD and

carers were more able to access a HCP or healthcare services when needed which is an important step in medicines management.

Another factor some participants spoke about was regarding the attitude of healthcare staff members. Peter (PWD, dyad) told me during their observation how 'as soon as I go into Boots. 'Hello D'. it is fantastic! They all know me in there. And all the shop keepers in that town know me. It's a lovely experience…and they all know that I've got this problem and they're very good about it aren't they Amy. they're all very good friends.' This example by Peter shows how PWD view a rapport to be important to their day-to-day lives and how it can affect their general experience when accessing healthcare. Jenny on the other hand had experienced GP staff who had seemed less caring of her medical history (cancer) and less concerned with building a rapport.

"It's [surgery] the worst I have ever, been to… I was diagnosed with cancer… just over 3 years ago…in that time… I had 1 telephone call. I had a letter, saying that the GP… my GP would like to… ring me on such a such a date which was about a fortnight away and I had a telephone call and he said er erm… right. I have had a letter and you've had this surgery and you're having chemotherapy erm… how is it? And I said 'well, I seemed to have recovered from surgery well thank you very much and chemotherapy seems to be going alright'. Oh good good good. Right thankyou. And that was it. And that's the only acknowledgement I have ever had from anybody up there that, that I have what in fact is a terminal illness eventually I mean." *(Jenny. Carer to PWD)*

Similarly, Bob and Jane had told me how they had also experienced a lack of empathy and additionally described how difficult it was to see a doctor.

"B: Yeah. You get the impression most the doctors have been there a long time they're just
J: Waiting. Waiting to retire yeah
B: There's no enthusiasm or interest there… but, actually, if you phone up for an appointment, and to actually see a doctor, you're lucky if you can see one within a week." *(Bob and Jane. Dyad where Jane has dementia)*

This lack of empathy and care described by Jenny, Bob and Jane could deter Jenny and others from accessing healthcare when people required it which could impact their medicines, healthcare and general quality of life.

*Experiences relating to the access of **medicines** from healthcare providers*

Accessing prescribed and non-prescribed medicines is a key part of medicine management and during these observations R heard about the various ways that medicines were ordered and collected to best suit the participant.

Participants who either had difficulty walking or lived alone tended to have their medicines delivered such as Sylvia who could not walk well and had her dossette box delivered once a week. Her daughter Debby explained how 'it just comes automatically every Thursday, one of the girls from the pharmacy will come along, deliver them'.

Others (both PWD and carers) who were more mobile preferred to go to the pharmacy or surgery themselves to collect and order their medicines. Harry (who lived alone) described to me how when he collects his medicines from the pharmacy down the road 'they give me, they give me er usually when I, when I've collected the medicines like I did yesterday, I've got another piece of paper er, a little card that says, my next, I can pick the next lot up on the 14th of February'. He then added how he puts his card with the date for next collection into his diary so that he knows when to collect his next repeat.

During Penny's observation, she described how not only does she require her dossette box from her healthcare provider, but she also used an external company to receive her colostomy equipment.

"It's a very very good system. Very good system. You can't fault it. You can ring them. They ring you and if you're out they leave you a message asking you to ring them back and err, they ask you if you want your usual order ad you say 'yes' and its delivered, you know within 2 or 3 days!" *(Penny. PWD who lives alone).*

This example shows how medicines management does not only cover conventional tablets and inhalers but also for some PWD involves using medical equipment. This adds another set of considerations for how PWD and carers manage their medicines.

Overall, these examples show how PWD and their carers find ways to overcome social, spatial and material factors for accessing their medicines (such as using a delivery service or by collecting in person) which were best suited to their current situations (such as being unable to walk easily).

In summary, the experiences described within this theme highlight how there are many factors which may affect how PWD access their healthcare providers and their medicines

such as being accessible, having rapport with the staff, feeling empathy from the staff and the ability to have medicines delivered. This theme also bring to attention how PWD can utilise various healthcare services such as delivery services in order to overcome some of the barriers which they may otherwise face with accessing healthcare.

5.5 Discussion

The observations highlighted how PWD and their carers used specific sequences of activities each day, often in the morning to help manage their day-to-day lives. These activities had become routine to the participants and mostly consisted of in-house activities such as waking up, going to the kitchen and making a drink. The observations attended to and recorded how these routines had been adapted by the participants to incorporate their medicines (such as waking up, going to the kitchen, making a drink, seeing tablets on kitchen surface, taking tablets) which could be classed as a form of domestication. 'Domestication' is a term used for the cultural integration of technical artefacts into the household and everyday life, with an emphasis on the process through which artefacts were appropriated and re-embedded in a local context when they were put into use [240, 241]. Thrall [242] builds on this by stating how consumers seek to incorporate new technologies into the patterns of their everyday lives to maintain both structure of their lives and control of that structure. A four-part process for domestication has been described where: (1) object is made physically available; (2) object is given a place; (3) object is incorporated into daily routines; and (4) household's cultural preferences were mediated to the outside world through the incorporated object [243]. Although here authors speak only of technical artefacts, this could also relate to other artefacts such as medicines in the home and described the process which patients undergo when they bring a new medicine into their everyday lives. It was seen clearly in the observation data how such a 4-part process was used: (1) new medicine is prescribed by the doctor and given to the patient; (2) PWD gives the medicine a specific place in the home (usually somewhere visible to help them remember); (3) PWD takes the medicine everyday as part of their new routine; (4) The cultural preferences of PWDs were shown to the outside world by how their medicine was incorporated into their everyday lives (such as through showing the researcher (an 'outsider') their medicine routines (cultural preferences) during the observations).

This theory shows how PWD adapt their routines within their homes as new medicines are brought into their culture and explains the types of routines which were observed in this project. Other studies have also reported routines to be a key factor in how PWD manage their daily lives. A study by Van Dijkhuizen et al. [244], examined how 9 women with early-stage AD made sense of, and attempted to cope with their situation and reported one theme to be familiarity. The women's connectedness with their environment and the use of well-rehearsed skills and routines helped the women to overcome their difficulties with episodic memory. Gathering information on a PWDs daily routine is therefore likely to be observed to be an important factor when assessing how PWD can successfully integrate anything new, including managing medicines into their lives and ensuring they can manage them safely within the home. To make it more likely that medicines are taken successfully and more effectively, pharmacists should therefore consider the established routines of PWDs (and carers) themselves, more closely and use this information to inform ways to plan how they could actively work with the PWD (or carer) to integrate their new or current medicines into their already well-founded routines.

Many of the PWD also had a range of support to help them manage their daily lives which included the management of their medicines. Two main types of support were identified. Physical objects such as dossette boxes, calendars, diaries, electronic buzzers and reminder notes and human support from informal carers, family, friends or neighbours.

Physical objects ranged from simple post-it-notes used for reminders across the home, to more complex dossette boxes and electronic emergency buzzers worn around the wrist or neck. As with the medicines, the physical objects were usually placed in visible places and were entwined into their daily routines (such as keeping the dossette box in the larder with the cereal). These observations showed how PWD had found methods and supportive objects which worked for them and their daily routines which enhanced how they managed their day-to-day lives and medicines. PWD and their carers should be informed by HCPs about the various types of physical support which is available to them and have the ability to choose which objects work best for them and their routines. In the case of the participants included in this small observational study, dossette boxes (made by both the participants and pharmacies) were seen to make a real difference to how medicines were effectively managed in the community. However, it should be noted that the use of dossette boxes are not suitable for everybody and they have been identified as a contributor to the £150m of avoidable medicines related waste each year in the UK [245].

The use of dossette boxes has previously been questioned and they have several limitations [246]:

- If a PWD forgets to take their medicines, it may be that the patient may more likely forget to take their medicine if it is in a dossette box
- Not all medicines can go into a dossette box such as medicines which have changing, when required or additional dosages (e.g. warfarin, painkillers, Sinemet), liquid and non-oral formulations (e.g. eye drops, nasal sprays) and medicines that are sensitive to light, moisture or temperature (e.g. Senna)
- Medicines can be difficult to identify in the boxes making extra administration precautions (such as take with food) difficult to apply and affecting a patient's choice to take their medicines.
- They may not be suitable for PWD and pose dexterity issues
- They are not tamper-proof or child-proof
- They may inadvertently improve the adherence of a PWD taking their medicines. This can lead to higher doses of a medicine (such as a medicine for diabetes) circulating in the body which can lead to adverse effects such as hypoglycaemia [247]
- Any medicines not taken in the box means medicines are wasted
- Extra workload for staff which is often done without any form of remuneration

Patients, carers and HCPs should keep these points in mind when deciding on the best form of physical support to help them manage medicines in the home and should only be advised to use a dossette box if appropriate medicines are prescribed and their use is regularly reviewed.

For those who lived with their informal carer, the carer was often observed to take responsibility for most or all aspects of the PWDs medicines. This can put great pressure on the carer as they are then responsible for the health and well-being of the PWD and when caring for a PWD, a carer's physical and emotional health has been known to suffer [86]. This study saw an example of how even a carer was having difficulties incorporating a new medicine into an established routine and in this instance, realised that she had forgotten to give the medicine to her mother the day before. The well-being of the carer and access to support to ensure the carers are confident that the PWDs medicines are taken as intended is therefore paramount for the successful medicines management of the PWD.

As polypharmacy continues to rise in people aged over 65 years [248], it was unsurprising to observe in many of the participants that they were having to incorporate not just one, but several medicines with differing times to be taken into their daily routines. This brings additional challenges to PWD as they need to order, collect, organise, store, and remember to take a variety of medicines which may need to be at different times of the day which could be confusing. The increased number of medicines increases the risk of medicine-related difficulties and side effects which could lead to medicines not being taken as prescribed, future complications and potentially hospitalisation. HCPs should therefore ensure that medicines are not prescribed needlessly and that dosing schedules are simplified where possible.

Even with large numbers of medicines, daily routine was found to be entwined in how participants managed their medicines. Different medicines tended to be placed in different areas of the home (such as kitchen, bathroom ad bedroom) in order for them to be visible during the times of the day in which they were required which helped the PWD or carer remember to take certain medicines at a certain time. This highlights again how important is it to identify a PWDs daily routine so that 'domestication' of a number of medicines can occur successfully at different times of the day.

Some of the difficulties observed by the participants with their medicines are difficulties which could be experienced by other PWD. The observation with Mary highlighted two difficulties of interest. Firstly, Mary was observed to have two white tablets which looked very similar but were for very different conditions and secondly, she was observed to have difficulty opening her Levothyroxine blister packs with her arthritic hands. At the time of the observation, Mary was aware of having two similar looking tablets and knew to be cautious with which one she was taking, but as the dementia progresses and her cognitive abilities decline, this awareness may reduce and Mary may begin to take the wrong tablet at the wrong time or not take them as prescribed which could lead to serious health consequences. Over time, Mary's arthritis may also continue to progress and Mary's difficulties with opening the blister packs may become so severe that she may not be able to get the tablets out at all which could also lead to serious health consequences.

The difficulties in opening packaging which Mary experienced is not specific to PWD and is not uncommon. Philbert et al. [249] reported that 1 in 4 patients (n=317) over 65 experienced difficulties opening their omeprazole packaging. Building on this, Williamson et al. [250] reported how in a qualitative study comprising of interviews with elderly

patients (n=32), concerns regarding the colour, shape, size, packaging, access and quality of the tablets were highlighted and how any changes to the medicine appearance (such as a different brand) threatened their controlled medicine management and caused them to question their routine. Mary's observation and the studies by Philbert et al. [249] and Williamson et al. [250] therefore raise how important it is for the brand, packaging and aesthetics of tablets being dispensed to PWD to be regularly reviewed and preferences documented to reduce the risks of future avoidable health problems related to the mismanagement of the medicines.

The side effects which were reported by some of the participants although severe in some cases, were in line with those listed by manufacturers [251] and the British National Formulary (BNF) [252]. The reality of how disturbing and frightening the visual dreams can be and recounted by one participant describing how she nearly stopped taking the medicine reinforces how HCPs need to ensure appropriate counselling of patients on the potential side effects of these medicines and what to do if they occur. These participants may have benefited from counselling from a HCP whose experience lies in medicines (such as a pharmacist) who could have provided expert advice to the participant. With this in mind, follow-up checks during the initial few weeks of being prescribed a new dementia medicine similar to those seen in the New Medicines Service (NMS) service (which has been reported to increase adherence by approximately 10% [253]) may allow the PWD time to try the new dementia medicine for a short time. Furthermore, it would allow them the opportunity to ask any questions which have arisen since being prescribed the medicine which may then improve their adherence and confidence in taking the new medicine.

Many of the observations showed how the various health conditions of the participants (both PWD and carers) affected the daily lives of the PWD which included the symptoms of dementia (such as confusion, forgetfulness and difficulties concentrating or holding a conversation) and other health conditions such as diabetes, high blood pressure, hearing problems and difficulties walking.

This study saw first-hand how the dementia caused simple tasks such as holding a conversation, answering the telephone, ordering medicines, collecting medicines and remembering and knowing what medicines to take being more difficult and often required the support of others. HCPs should therefore be aware of the dementia symptoms,

communicate to them appropriately and offer ways to overcome any difficulties being faced by the PWD or carer.

Other health conditions (such as difficulties with hearing or walking) were also seen to affect the day-to-day lives of PWD during these observations which also impacted how medicines were managed (such as the inability to collect medicines in person or speak to the surgery on the phone). The prevalence of comorbid conditions in PWD is known to be high [254] and so the large number of comorbidities experienced by the participants was as expected. This means that PWD are at risk of not being able to access the healthcare they require when they need it (such as for diagnosis and treatment or the review of medicines) and may benefit from further support which could be provided by their community pharmacies.

In addition to the PWD having comorbidities, the informal carers were also found to be prescribed medicines for themselves, for various comorbidities. This was also an expected finding due to the older and mainly female demographic characteristics of the carer group who have been shown to be prescribed an increasing number of medicines over time [255]. In the observations, carers were often found to be managing both their own and their PWDs medicines, which involved the 'domestication' of all of the household medicines into their daily routine to ensure that neither the carer's own, or their PWDs medicines were forgotten. This extra responsibility observed in many of the dyad observations may increase the burden experienced by the carer and highlights how the carers may also need more practical or emotional support. It also raises the concern regarding what happens if the carer is unable to support PWD with their medicines (such as having an operation or chemotherapy treatment) which was a true experience described by one couple. The carer is then not only having to undergo potentially high-risk procedures but has the responsibility to ensure that there is alternative support in place to ensure that the daily life and medicines management of the PWD is minimally affected. Carers of PWD should therefore have the information made available to them of external support which may entail the provision of help for such instances as hospital visits, mental well-being or someone to talk to.

This study found how participants' experiences of access to healthcare providers such as GP surgeries and pharmacies varied. Some had experienced friendly staff who were aware of their condition or knew their name and had as a consequence built a good rapport between themselves and the staff which made visiting the surgery or pharmacy as pleasant

experience. The surgery being physically accessible due to a flat car park and lots of chairs and the accessibility of user-friendly practice nurses were also factors which led some participants to more pleasant experiences which encouraged them to access and use their services.

Conversely, some participants described experiences which may reduce their future access to healthcare. The lack of empathy Jenny experienced from her GP surgery has caused her to not regard her surgery highly and felt less inclined to use their services. This experience highlights how small gestures such as showing empathy and a caring attitude towards patients can help make a patient feel valued and be more inclined to access and use the service. If these services were not accessed by PWD and their carers, then processes such as the diagnosing, prescribing, ordering and collecting of medicines may not occur which could jeopardize the health and well-being of the individual. Therefore, factors which encourage PWD to access their healthcare providers should be considered such as dementia friendly environments, dementia trained staff who are empathetic and ensure their patients feel valued, plenty of seating and appropriate HCPs available for appointments.

The access to and the collection of medicines is a key part of the medicines management process and this study showed how each participant had tailored this aspect to meet their requirements. Some of the participants were more able and preferred to visit the pharmacy to order and/ or collect their medicines in person, whereas some of the less mobile relied on a delivery service which, in 2 cases, was a regular automatic delivery of a dossette box. This shows how the needs of PWD are different and their ability to collect their medicines can be affected by a number of factors such as their memory, mobility and presence of an informal carer. An intervention should ensure that there is a clear plan for how medicines will be ordered and collected which suits the PWD and carer as this is an essential aspect to medicines management.

Strengths and Limitations

Complying systematically with the criteria of Lincoln and Guba, for ensuring rigour [234] within this study ensured high quality findings for this study. The triangulation of data sources ensured credibility, thick descriptions of the observations with the addition of photographs within the expanded accounts ensured transferability and the continuous use of a research diary and use of recruitment and observation log sheets ensured dependability and confirmability.

Another strength to this study was that the research protocol was initially sent for peer review at a local research peer review committee (excerpt in Appendix 34) which ensured that the study was designed appropriately to that all aspects which needed consideration had been considered. This led to a robust study design being developed which would be able to be implemented successfully in the local NHS trust and the successful application of the study to both HRA and REC.

The participants were a mixture of dyads and those that lived alone and a mix of genders were included which allowed a wide variety of data to be collected and provide a more well-rounded view of the current way that PWD and their carers manage their medicines in their homes.

The decision to take a 'moderate participation' stance was also a strength to this study as it allowed the researcher to interact with the participants with minimal disturbance to their usual routine. The ability to interact with the participants enabled the researcher to ask questions relating to what she was seeing and therefore gain more information regarding what the participants were doing and why. It also allowed the researcher to gain information on subjects relevant to the research question but were not necessarily being observed at the time such as the participant's experiences with their GPs and pharmacies. This stance therefore provided the researcher with the opportunity to gain a wide variety and depth of knowledge which would not have been possible with other stances such as 'passive participation'.

Conversely, although using the 'moderate participation' stance meant there was the possibility for bias to be introduced as the participants had the opportunity to modify their behaviour and their usual routines. However, as documented in my research diary, my naturalistic demeanour led to me building good rapport with each participant both before and during the observations which was evident from the relaxed atmospheres experienced during each observation. Participants appeared to enthusiastically allow me in various rooms of their homes including bedrooms and bathrooms and seemed to be honest about their thoughts regarding their primary care experiences, which suggests that the participants felt at ease in my presence and without pressure to hide information from me. These factors helped to ensure that I observed or heard accounts of a variety of experiences which enriched the data collected and increased the credibility of the research findings.

Although I took thought and care in designing and implementing the recruitment and consent procedures for this observational study, there were limitations, particularly the recruitment bias perhaps introduced by the nurses doing the initial screening for potential participants. Nurses may have only selected patients whom they judged to be more confident and likely to take part in the study rather than asking all patients that met the criteria. Although the achieved study sample was diverse, recruitment bias may have narrowed the spectrum of participants involved.

Additionally, the majority of participants were generally managing their medicines appropriately in their homes. This could be because perhaps the majority of people with mild-moderate dementia were managing well with their medicines, but it could also be that patients not managing well with their medicines were less inclined to initially consent to the nurses for the researcher to tell them more about the study. Again, this led to a less diverse sample within the study which makes the results less transferable.

Another limitation for this study is that although there were two recruitment sites and a total of six nurses involved in the study, due to staff sickness and workloads, one of the sites was not recruiting for a large proportion of the study period and at the other site only one of the nurses was actively engaging in continuously screening patients for the study. This could have reduced the range of participants that were screened for this study which in turn could have led to potentially less diversity within the sample.

Although the focussed ethnography enabled the medicines management of PWD to be studied in the context of their own homes, the short, singular observations could not provide any observational data relating to how medicines are managed over a longer period of time or outside of the home such as visiting the GP or pharmacy and the collection of their medicines. These are key aspects of medicines management and although the participant's experiences were described to the researcher during the observations, the data could have been enhanced in terms of depth and fuller understanding of participants' everyday routines and social support by incorporating some longer or multiple visits to the participants which included visits to primary care sites.

5.6 Chapter 5 conclusions

The results from this observational study have both built on the findings of the previous chapters and added a new dimension by allowing data to be collected in context and from the people that this study aims to support further.

Some of the data found in this observational study expands on what has been previously identified in previous chapters. Chapter 2 identified a number of medication review based interventions for PWD and the case-control study in Chapter 4 determined that there was a range of co-morbidity risk factors for PWD developing pneumonia. This study built on these results by observing how many PWD and carers are managing a number of different medicines and formulations for a range of co-morbidities which partly explains why medication reviews were the intervention of choice for many of the studies in chapter 2.

The observations provided new information which would otherwise have been unknown such as:

- The importance of routines
- The varying methods of support used and the involvement of the informal carers
- How difficult day-to-day tasks can be for PWD
- The range of experiences people affected by dementia had received in primary care and how this had affected their access to healthcare and their medicines

This observational study found how PWD and their informal carers incorporated their medicines into their daily routines which often involved placing the medicines in a place which was visible during a certain time of their daily routine so ensuring that the medicines were taken at the time intended by the prescriber. A community pharmacy intervention could therefore include identifying how medicines can be incorporated into already established routines and this has been added to the logic model (Figure 23).

Support for managing medicines was an important factor for PWD and their carers who often had a number of additional health conditions and medicines which could further impact their daily lives. A variety of methods were observed which enabled the PWD to continue to live and manage their medicines successfully within the community. For these reasons, the intervention could include reviewing and identifying potential support mechanisms for the carer and PWD, a comprehensive review of the medicines including the appropriateness of all medicines and assessing any problems with packaging and aesthetics. The medication review should also involve counselling on the medicines and

their potential side effects and appropriate signposting for further support where needed. These elements have been added to the developing logic model (Figure 23).

PWD and their carers had varying experiences of their healthcare providers and used different methods to access their medicines to suit their circumstances. Community pharmacies should be aware of the need for flexibility in how medicines can be ordered and collected to suit PWD and the intervention could include a review of how medicines are ordered and collected. The intervention could also review and identify if and how dementia symptoms and other health conditions are impacting on daily life and accessing healthcare and provide strategies for improving the PWDs access to healthcare if needed. Part of this is also ensuring that the pharmacy layout and staff are dementia-friendly. The intervention elements of reviewing how medicines are accessed and how the dementia impacts on this access and having a dementia-friendly environment have been added to the logic model (Figure 23).

This study highlighted how informal carers are often heavily involved in the everyday running of a PWDs life which includes managing their medicines. Community pharmacy staff should be aware of this and a future intervention should ensure that with the permission of the PWD, the carer is involved in all aspects of the intervention and also receives care and support themselves. This aspect has also been added to the logic model (Figure 23).

Problem	Context	Inputs	Outputs	Process measures	Clinical outcomes	Humanistic Outcomes
Dementia prevalence increasing Limited support in the community for PWD Pneumonia is a primary cause of hospitalisation and death in PWD	Co-morbidities Polypharmacy Carer burden Inappropriate medicines	-Medication review -Targets medicines (e.g. antipsychotics) -MDT + signposting -Time efficient -Varied training -Use of a tool - Replicable -Manage risk factors for pneumonia -Dysphagia screening -Formulation appropriateness -Manage ALL co-morbidities (including polypharmacy, side effects and impact on daily life) -Address aesthetic or packaging concerns -Management of ALL HOUSEHOLD medicines -Routines -Physical and human support -Counselling and signposting -Access to healthcare and medicines -Dementia friendly	↑ Engagement Effective referral Pathway ↑ MDT relationships	Number of Medicines ↑ Medicine Appropriateness ↑ Confidence And Knowledge ↑ Adherence % of changes accepted Improved access to healthcare and medicines	↓Hospitalisation ↓ Mortality ↑Cognition ↑dysphagia diagnosis	↑Number living in community ↑ QOL Patient satisfaction
	Community pharmacy current lack of knowledge and skills regarding dementia Pharmacist role evolving Pharmacist supports other conditions such as asthma but not dementia Pharmacies are accessible. Often operate in isolation	Patient participation Carer involvement	↑ Awareness of pharmacy role/ skills and intervention Time to talk to an accessible HCP Feel more in control about medicines management Improved management of co-morbidities Time to think of ways to overcome current barriers	Quality of documentation ↑ Skills and Confidence Time takes	↑ Clinical knowledge	Job satisfaction

Assumption: Community pharmacy can improve medicines management of PWD and reduce pneumonia risk which will lower hospitalisations

Key: PWD/ Carer ● Primary care staff ●

Figure 23. Completed logic model following observational study

Chapter 6

Study discussion

6.1 Revisiting the aims and objectives

In chapter 1, the aims and objectives for this study were outlined and were as follows:

Aim

The aim of this study and PhD is to develop the evidence base and theory to underpin the development of a community pharmacy intervention which supports and enhances the medicines management of people affected by dementia and who live at home in the community.

Objectives:

1. To identify the types of interventions that have already been trialled in PWD which use members of the pharmacy team and their effective and ineffective elements.
2. To identify any potentially modifiable risk factors for pneumonia within a community pharmacy setting.
3. To explore how people with mild-moderate dementia are currently managing their medicines at home within the community without the help of a paid carer.
4. Complete a logic model for a proposed community pharmacy intervention.

The SR, nested case-controlled study and observational study highlighted numerous ways that community pharmacy could intervene in order to enhance the medicines management of people with dementia. In this discussion, the key points from the earlier chapters are revisited and brought together to provide recommendations for what could be included within a community pharmacy intervention.

6.2 Strengths and limitations of this study

This study provides an array of evidence for how not only community pharmacists, but all HCPs could provide better care and support to PWD. This means that much of this thesis is relatable to a large audience and many of the recommendations below could be transferrable in many settings and with many HCPs. This in turn means that a larger number of PWD could be better supported in how they manage their medicines.

The SR provided a good baseline for assessing the current interventions targeted at PWD which could be provided by community pharmacists but provided limited insight into the effectiveness of the interventions due to the low quality of the studies included.

The case-controlled study provided further evidence for certain risk factors for developing pneumonia in dementia. This study also generated new evidence by exploring the relationships of different formulations with developing pneumonia. Although the formulation results reported are not conclusive, it is a start to an otherwise unexplored area of research which warrants further investigation. However, the associations between the various risk factors and pneumonia, which were reported, need to be reviewed with care due to the quality of information within the database being questionable as detailed within chapter 4.

The observational study using ethnographic methods more directly and accurately explored how PWD living in the community for the current situation actually managed their medicines in practice which had otherwise not been directly evidenced. This study provided real insights into types of ways PWD and their carers directly manage medicines and ways and means they overcome a variety of specific barriers that PWD can face in their day to day lives, which might not otherwise be known to community pharmacists trying to support them to do so. This study was however conducted in just one small area of the UK and the observations and experiences reported here may not reflect the experiences relating to medicines management of other PWD in other areas.

Although three very different study designs were used within this study to provide a comprehensive overview of how community pharmacy could enhance the medicines management of PWD, there were a number of areas, which were not explored which would be important to factor in during the development of a future intervention. These include the voices of the patient and carer regarding their preferences for a future intervention, the community pharmacists' voice, the GPs voice and the voice of any other HCPs which may be involved. Additionally, the practicability and feasibility of an intervention in the current climate are unknown and would need significant consideration.

The completed logic model Figure 22 at the end of chapter 5 provides us with a starting point for developing new services and designing research projects. The next step is therefore to present this to practitioners and patients to obtain their views on the theories and different inputs they would like to see within any service.

6.3 Key findings

This study reports new information on how people affected by dementia could be supported by community pharmacists to both improve their quality of life and reduce risk

associated with their treatment. We now also have well-contextualised, detailed insights into how both PWD and their informal carers currently manage their medicines within the community. A range of key findings from the three research projects have the potential to shape a future more appropriate dementia support service (DSS) for use within community pharmacies.

The systematic review in chapter 2 reported how many of the interventions were medication review based. Community pharmacists are well trained and practiced in conducting a certain form of medication review called a 'medicines use review' (MUR) which focuses on adherence and lifestyle.

Community pharmacists are encouraged to adhere to four medicine optimisation principles to enable a patient-centred approach to care [89]:

1. Aim to understand the patient's experience
2. Evidence based choice of medicines
3. Make medicines optimisation part of routine practice
4. Ensure medicines use is as safe as possible

The adherence support covered in MURs only meets a small part of this recommended approach to care and our results suggest that a much broader intervention is required which could meet all four principles. Furthermore, taking into account criticisms levelled at the delivery of MURs and their quality, which is partially associated with the lack of training to underpin them, there is a need for a new medicines review model, with significantly more care taken in developing, introducing and implementing any new service [256, 257].

A community pharmacy dementia support service (DSS) would include a number of different elements relevant to people affected by dementia in order to optimise their medication. These are described below and summarised in the completed logic model (Figure 22).

6.3.1 Emphasis on certain medicines

Several of the studies included in the SR in chapter 2 concentrated on the anticholinergic burden found during polypharmacy from such medicines as antipsychotics, anticholinergics and benzodiazepines, as they are known to have adverse effects in the elderly and PWD [163, 164]. The results from the case-controlled study in Chapter 4 built on this knowledge as the use of antipsychotics in PWD were reported to be associated

with an increased chance of developing pneumonia which can lead to hospitalisation, dementia progression and death.

The DSS could therefore target or have particular emphasis on an agreed list of medicines which are known to cause potential unnecessary harm to PWD. This list could include anticholinergics, antipsychotics and benzodiazepines. The DSS could check for the appropriateness of the medicine and dose prescribed, side effects and prepare individualised care plans outlining expected outcomes, proposed monitoring for effectiveness and side effects plus the next formal review date. Providing community pharmacists are aware of current guidelines and are trained to identify both patient improvements and side effects they could provide significant additional support both at the point of medication initiation and during any attempts to deprescribe.

For community pharmacists to be able to effectively implement this, without duplicating the work of others in the primary healthcare team, they would need access to the patient's records, a good working relationship with the patient's GP and preferably the ability to make the changes themselves.

6.3.2 Management of multi-morbidities

The observational study reported several of the participants being prescribed several medicines for different conditions. Although not observed in chapter 5, COPD is one condition which is commonly seen in the community and will affect many PWD. The case-controlled study in chapter 3 found that PWD and COPD were associated with twice the chances of developing pneumonia compared to PWD without COPD. This result shows how other morbidities can also cause serious further health complications for PWD and how important it is that the DSS not only checks whether the symptoms and progression of dementia are being managed appropriately, but whether the management of their other morbidities (such as COPD) are considered (such as checking inhaler and spacer technique, ensuring that the dose and strength of medicine is appropriate and the discussion of smoking cessation where required [258]. Although in an ideal world, the DSS would include all suggested elements, it is, in practice, not realistic or possible. Therefore, although it would be beneficial for community pharmacists to undergo refresher training on the management of co-morbidities such as COPD as part of the training for the intervention, this should only be included if practically feasible and once all other training aspects have been chosen and prioritised.

6.3.3 Dysphagia identification and formulation

The case-controlled study in chapter 4 reported an overall prevalence of dysphagia within PWD of 4.15% and so although the prevalence of dysphagia is potentially low within community settings (compared to institutionalised settings where it has been reported to be as high as 45% [45]), community pharmacies regularly experience patients with a swallowing disorder. Two reasons for this may be because dysphagia is not routinely screened for in this population and when it is identified it may not be recorded using specific READ codes. The DSS should therefore include prompts for the pharmacist to check for any signs of dysphagia such as: difficulties swallowing medicines, weight loss, coughing or gagging on swallowing and having a sensation of food/medicines getting stuck in your throat or chest [36, 259]**.**

The high association of liquid medicines and developing pneumonia in PWD also reported in chapter 4 highlights how simply switching a dysphagic patient to a liquid medicine may not always be the most appropriate solution and all formulations should be considered. Where a liquid formulation is to be used, viscosity should be tailored to suit the individual. Care should also be taken when using thickeners with medicines as research suggests that in certain circumstances efficacy can be significantly reduced.[260].

To ensure that the most appropriate formulations are prescribed for any potential dysphagic patients, the DSS should have a procedure in place for the referral of patients to a SALT for further investigations and the ability for the pharmacist, doctor and SALT to work together to find the most suitable solutions.

For this aspect to be included, community pharmacists would need further training which includes what dysphagia is, how to identify it, how the referral process works and how to work with other HCPs to develop a medicine care plan with appropriate formulations.

6.3.4 Medicine packaging and aesthetics

During the observational study, it became apparent how similar looking tablets, changing shapes and sizes of tablets and packaging can cause confusion and unnecessary worry or potential harm to PWD. With pharmacies continually being supplied with a variety of generics from their wholesalers, it is important to remember how these changes may have an impact on PWD. The DSS could include a prompt for the pharmacist to ask the patient specifically about the aesthetics and packaging of their tablets and whether the patient is experiencing any problems. Most community pharmacists will be unaware of

these difficulties and therefore approaches to raising awareness of this problem, which is relatively simple to address, are required.

6.3.5 Involve and support the carer

As the observational studies showed, carers of PWD can often be the ones who manage the medicines for both themselves and the PWD. With this knowledge and the fact that many carers experience carer burden which can be unacknowledged by HCPs [261], it is important that the carers are equally supported in the management of medicines in their homes. NICE guidelines state that there should be support for carers of PWD with the inclusion of appropriate information and signposting to ensure carer and PWD well-being [77]. A community pharmacy DSS should support the findings from chapter 5 and the NICE guidelines by ensuring that where the PWD has an informal carer, they are supported and included in the service. This can be achieved in a number of ways:

- If both the carer and PWD are present in the pharmacy, then the carer should be invited in with the PWD to the DSS (with their consent where capacity is able).
    - The questions should be posed to both PWD and carer to ensure comprehensive picture of medicines management at home.
    - Answers and further support or signposting should be offered to both PWD and carer.
- If the carer is present at the pharmacy on their own and the PWD never comes to the pharmacy, the carer should be invited to the DSS on their own.
    - Their role with medicines management will be identified and the appropriate questions asked.
    - Advice, further support and signposting will be offered.

This recommendation not only assumes that community pharmacists have the skills to effectively deliver such interventions but the sensitivity to include the carer with the patient present and an ability to effectively assess for capacity and adhere to the laws surrounding it. These may therefore be additional training needs.

6.3.6 Routines

The observational study highlighted the importance of recognising everyday routines for both PWD and their carers and how these routines were, over time, amended to integrate or ‘domesticate’ their medicines, which ensured that medicines were taken as prescribed. For medicines to be incorporated successfully into the PWDs daily lives, it is therefore important that the current established routine is known. During the DSS, the

pharmacist could work with the PWD and/or carer to ensure that the medicines are taken as intended and if needed, provide suggestions based on the usual daily routine for how the medicines could be better integrated to fit in with their lifestyle and improve adherence. To provide a fully comprehensive service to the patient, the DSS could have an option included for the community pharmacist to visit the PWD and carer at home where routines and current management of medicines could be seen more in context.

Pharmacists visiting homes would however introduce additional costs. With new interventions being required to demonstrate a cost per Quality-Adjusted-Life-Year (QALY) of less than £20,000 [262], it is therefore important that new interventions demonstrate good value for the NHS. Consequently, this means that robust research to determine the cost and effect on QOL is required to enable the QALY calculations to be performed.

6.3.7 Support

A variety of methods of support were utilised by participants during the observational study. These ranged from the use of dossette boxes, reminder methods and the use of the carer or close family members. These support mechanisms were seen to be an integral part of how PWD managed their medicines within the home and is another aspect which the DSS could include in order to ensure patients have access to and are receiving the support in which they need. Community pharmacists should therefore ensure they are aware of all the specific and relevant support options available to individuals in each case and that they have the necessary training and strategies in place to ensure that they can be implemented effectively. Community pharmacists would need to have acquired the skills to identify those additional support needs and be able to provide individualised advice and support based on each patient's needs and preferences.

6.3.8 Everyday difficulties with dementia

As described during Chapter 5, PWD are often experiencing a variety of difficulties. Some due to age (such as hearing) and some due to the dementia (memory, speaking, doing simple tasks). The observations saw how these difficulties can make managing medicines more difficult (such as contacting the surgery and collecting medicines) as they may find it difficult to order, collect, organise and take their medications correctly or to visit an HCP when they need medical help. The community pharmacist has the ability to ease some of these difficulties (such as signposting for hearing tests or additional support), offering medicine deliveries or the automatic dispensing of their regular medication and so the DSS should review any additional difficulties which the PWD may be experiencing and

offer solutions or referrals where required. Some of these possible solutions however are associated with extra costs (such as delivery of medicines) and so the variety of options available would need to be carefully considered and staff informed of these options to ensure that the DSS is cost-effective and seen to be beneficial to commissioners.

6.3.9 Use of the Multidisciplinary Team

The SR in Chapter 2 reported that the use of a Multidisciplinary Team (MDT) which included a pharmacist were effective elements to the interventions. As the role of the pharmacist continues to evolve, community pharmacists are well placed to work with other primary care HCPs to provide a more streamlined and comprehensive level of care to PWD. For the DSS to be effectively implemented and be of greatest value to PWD, an interdisciplinary team should be involved with the development of the service. This will also ensure that the service is of maximum benefit to the HCPs as, for instance, the DSS could be designed to work with GP Quality and Outcomes Framework (QOF) targets, reduce GP and nurse workloads and improve the use of medicine budgets.

Designing the DSS with all HCPs in mind will also align with recommendations within the Murray Review [105] for the successful implementation of community pharmacy services which include:

1. Build local relationships based on trust, especially with GPs
2. Build routes of multi-professional training
3. Enable shared clinical records and the ability to effectively communicate with the rest of the clinical team
4. Develop formal referral pathways between GPs and pharmacy to ensure patients are managed well
5. Focus on patient care and develop incentives to facilitate pharmacist and GP engagement
6. Raise awareness of the service and provide easier access to information about the service
7. Use campaigns to inform public of the role of the community pharmacy in managing ill health (or in this case dementia)
8. Work with patient groups to ensure that the service meets the need of the service user
9. Develop a training and mentoring framework to support the development of enhances clinical skills

Recommendation 5 is of particular importance as the developed logic model (Figure 23 already includes outcomes which could be used as incentives to the community pharmacists and GPs to facilitate their engagement with the service (such as job satisfaction, improved patient QOL and improved clinical knowledge).

6.3.10 Continual support

Unlike many current services in community pharmacy, the DSS would ensure that continual, ongoing support is available to people affected by dementia. This would be because, as heard during the observations, circumstances can often change for PWD as the disease progresses and the amount of support required increases. DSS would therefore be a service which would allow PWD and/or their carers to speak to the pharmacist for additional help or support at any time.

6.4 Barriers to the DSS

In addition to the training needs and potential additional costs identified throughout this discussion, other barriers to implementing such as service as the DSS were identified in the Murray Review [105] which include: Poor integration of the pharmacy workforce with other parts of the NHS, issues around behaviours and cultures (including sometimes weak relationships between GPs and pharmacy) and system design issues.

6.5 Enablers of the DSS

To overcome the potential barriers described above, the DSS also had a number of potential benefits for both PWD and HCPs (summarised in the completed logic model, Figure 22), which could be used to promote the service to commissioners.

Benefits to PWD

PWD may have a greater understanding and management of their co-morbidities and medicines and may be more aware of methods that can be used in dementia to help them to manage their medicines effectively. This may lead to an improved quality of life for both the PWD and informal carers, reduced visits to the GP surgery and reduced number of hospitalisations and mortalities from complications such as pneumonia.

PWD and their informal carers may also have improved access to a range of information and support tailored to them, such as other dementia services and methods for improving medicine adherence in dementia which otherwise may be difficult to source.

Benefits to GPs

The DSS may ensure that only medicines appropriate to the patient are prescribed which may lead to a reduction in the number of medicines prescribed, which may help GPs to meet certain QOF targets such as reducing the number of antipsychotics prescribed.

GPs may be able to use their appointments more effectively and see patients more in need of their expertise if PWD can access information from the DSS which would conventionally have needed a GP appointment.

Benefits to community pharmacists

Staff may acquire new knowledge and skills, have the opportunity to build a better rapport with some of their patients and allow their expertise and job role to be promoted within their community. This may in turn create greater pharmacist job satisfaction as increased clinical involvement, contact with patients, collaboration with physicians and opportunities to use professional skills have all been previously shown to increase pharmacists' satisfaction with their job and profession [263-265].

Following the steps reported in the Murray Review should ensure that the developed intervention is comprehensive, effective, implemented successfully, well accepted within the community and provides maximum benefit to people affected by dementia who are living in the community.

6.6 Future work

Carrying out this research design with a focus on PWD was a novel method for exploring how community pharmacy can enhance the medicines management of PWD. It has highlighted the relevance of using a mixed methods approach, as used here, to improve the knowledge of how PWD manage their medicines and how they can be further supported.

Although this research reported several key learnings that will help in the development of the DSS, several questions have also emerged that will require further research as part of the intervention's further development. Table 50 summarises these key learnings along with the questions that have emerged.

Table 50. Future work to DSS based on key learnings

Key learnings from study	Further questions for DSS
PWD would benefit from medicine reviews which target specific medicines	Which medicines to target for maximum effect, methods to record consultations and designs of intervention guides
Intervention would be most effective with good relationships and use of MDT	Which members to involve and when to involve them, how best to communicate with them, identification and addressing of barriers and enablers to effective interprofessional working
Community pharmacist would benefit from comprehensive training	Which training methods are most effective and cost-effective. What to include in training materials.
Dysphagia requires identification and management	Methods of dysphagia identification that can be used in community pharmacy. Referral strategies.
Liquids require consideration of consistency	Community pharmacists' current knowledge base.
Comorbidities (Such as COPD) need ongoing review and management	Which co-morbidities to include and the feasibility of including their review and management.
PWD would benefit from: Diverse support, medicines to be successfully incorporated into daily routines, access of healthcare to be considered and difficulties with medicines to be identified	The potential cost-effectiveness of all options available to community pharmacists. Availability of options as these may differ location dependent.

To answer these questions and further develop and implement the DSS, a number of steps should be completed, and these are outlined below:

1) Discuss the DSS from the point of view of key stakeholders

The thoughts and opinions on a future DSS need to be sought from a variety of other key stakeholders to answer some of these questions in Table 50 such as: GP staff, community pharmacy staff, local commissioning groups and the service users. This could be done by way of focus groups, interviews or a questionnaire.

It is not possible for the DSS to include all potential elements identified from this research. Using whichever method, one key question that needs to be discussed by the stakeholders is regarding which elements would be the most cost-effective and of most benefit to patients to be included in the DSS. This stage is therefore important as it will help to identify which elements are most important and feasible from the point of view of the stakeholders and which ones to continue to develop as part of the DSS.

2) Create learning materials and DSS resources

Once the elements to be included in the DSS have been chosen following the stakeholder consultations, learning resources need to be designed and created for the staff who will be involved in the DSS. Resources such as a DSS checklist tool, referral forms and consent forms may also need to be designed and staff trained how to conduct the DSS.

3) Pilot the DSS

A couple of local pharmacies and GP practices who are enthusiastic about the intervention will be used to pilot the DSS. The pilot will be used to check if the DSS is practical and feasible and whether any additional learning materials or resources are required. Ongoing feedback from both the staff and service-users will be sought via questionnaires and focus groups/interviews. This step is in line with the MRC recommendations for designing a complex intervention [92] (Figure 24).

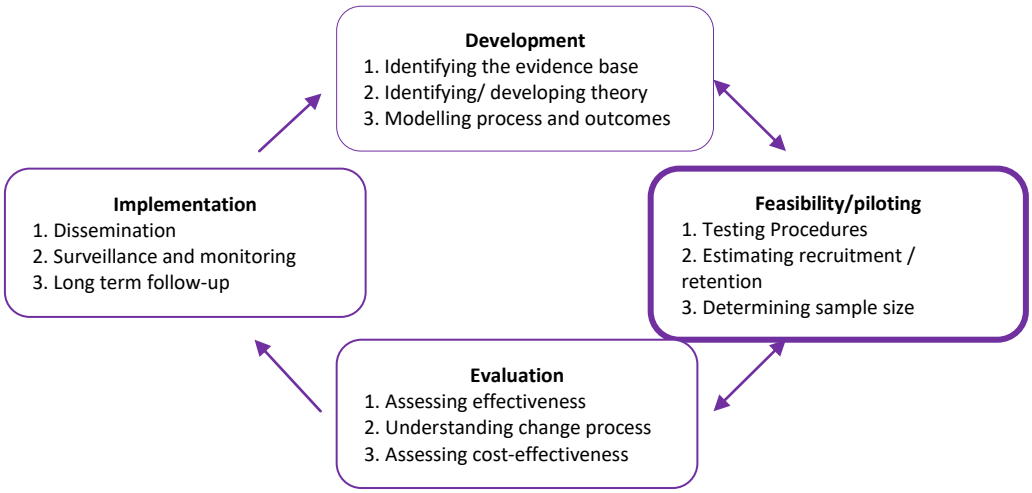

Figure 24. MRC process summary for developing a complex intervention

4) Amend the DSS

Dependent on the feedback from the staff and patients, amendments may be made to the DSS. This may be which elements are included, what training is required, what resources are needed, how the staff are remunerated (if they are) and how patients find out about the service.

5) **Repeat steps 3 and 4**

The DSS will then undergo a cycle of pilot and amending until the service receives positive feedback from staff and service users.

6) **Conduct an RCT**

Ideally, the DSS should then be tested for cost-effectiveness, clinical effectiveness and patient benefit with the use of a high-quality RCT with clearly defined economic, clinical and humanistic outcomes. The RCT would test the DSS against patients with usual care. The results from this RCT would determine whether the DSS in its current state could be enrolled out to pharmacies.

If the outcomes were not positive, then the previous steps would be re-visited and amendments made.

7) **Enrol pharmacies into the DSS**

The DSS will be introduced to a number of CCGs and staff recruited and trained to have the DSS in their pharmacies. Ideally, over time, the majority of pharmacies across the UK will be competently conducting the DSS and PWD benefiting from a local and accessible service.

8) **Intermittent service evaluations**

A random selection of pharmacies will intermittently undergo service evaluations of the DSS using questionnaires for both staff and service-users to ensure continued quality of the service and benefit for PWD.

6.7 Final conclusions

Although it is not be possible for the DSS to include all of the proposed elements identified through this research, the findings from this study have highlighted several key elements which **could** be incorporated into a DSS to enhance the medicines management of people living with dementia in the community and are summarised in Figure 25.

The DSS could:

1. Pay particular attention to antipsychotics, benzodiazepines and anticholinergics and check for appropriateness, side effects, unnecessary anticholinergic burden and patient's awareness to any potential risks.
2. Review ALL of the PWDs medicines and morbidities for appropriateness, technique (where applicable) and overall management (such as reviews with other HCPs).
3. Identify any potential swallowing problems and have procedures in place to refer to SALT. Where swallowing problems are found, medicine formulations could be thoroughly reviewed by the pharmacist, SALT and GP and be tailored for the patient.
4. Involve the PWD being asked if they have experienced any problems or have concerns regarding the aesthetics or packaging of their medicines with solutions being found where possible.
5. Involve the carers of PWD and ensure that they feel supported with all aspects of both theirs and their PWDs medicines.
6. Explore the adherence and incorporation of the medicines into the PWD (and /or carer's) daily routine with practical suggestions for improvement made where needed.
7. Explore with the PWD (and/or carer) how they are being supported and if they could be better supported with managing their medicines. This should include the use of physical objects and human support.
8. Check if the PWD is experiencing any difficulties with accessing healthcare and any other aspect of managing their medicines which has not previously been explored. Solutions could be found where difficulties are found (such as the delivery of medicines or referral to an audiologist).
9. Make use of the expertise of a variety of HCPs and have effective referral pathways and communication in place.

10. Involve continual support to the patient.

To deliver such a service, there are likely to be a number of training needs which may include:

Knowledge:

- Overview of dementia - *what it is, it's symptoms, how it progresses, how it affects the person and those around them*
- How AChEIs, memantine, anticholinergics, antipsychotics and benzodiazepines - *work, interact and affect PWD*
- Local and national knowledge of other dementia support services – *e.g. Alzheimer's Society, dementia cafes, local hearing clinics, carer support services*
- Dysphagia, importance of appropriate formulations and which HCPs are involved and what they do (e.g. SALTs)
- DSS procedures such as consent, conducting the service and referrals
- Helpful resources that can be used during the DSS such as the website www.swallowingdifficulties.com which has advice on the different formulations of medicines and when they can be used
- Potential signs of abuse of PWD and signs of PWD being uncomfortable or showing signs of anxiousness during the service but being unable to communicate it

Skills:

- Building and maintaining an effective relationship and rapport with the PWD and carer
- How to integrate the carer into the discussions
- Assessing for capacity and ensuring informed consent

Attitudes:

- Being engaged and believing in the DSS
- Pharmacist feeling comfortable and confident with conducting DSS
- There are no preconceptions or judgement of PWD from pharmacy staff and that patients are treated fairly

Incorporating these aspects into a comprehensive training package will ensure that community pharmacists are confident and have the evidence-base to provide an effective and beneficial intervention to PWD and informal carers who live within the community and help support them with their medicines.

Figure 25. Summary of recommendations to include in pharmacy intervention

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Appendices

Appendix 1. Scoping review method

Inclusion criteria

The inclusion criteria was set for the scoping review by using the PICOS (Population, Intervention, Comparator, Outcome, Setting) method as suggested in the Cochrane guidance [127].

Population

Any intervention which exclusively involved patients with dementia in any way were considered. This included people with dementia and the carers or family members of someone with dementia.

Intervention

The intervention was required to be conducted by a member of a community pharmacy team including pharmacists, dispensers, accuracy checking technicians and pharmacy assistants. Where the intervention was conducted by a multidisciplinary team, the pharmacy team member was required to have a key role in order for the research to be included.

Comparator

No comparators were applicable for this type of review.

Outcome

There were no set outcomes due to the nature of the research aims and objectives but each studies' outcome measures and results would form a key part of the data to be extracted.

Setting

The setting was restricted to community pharmacy. If multiple settings were used, the majority of or key aspect of the intervention was required to be set in a community pharmacy.

Types of studies

All study designs were included and any form of published data would be accepted. This included conference abstracts, service evaluation reports and research journal articles.

Studies were included for both reviews from any country and in any language (as long as the data could be translated) and from any date up to the date that data screening occurred. The broad inclusion criteria was to ensure that every potential intervention was captured.

Exclusion criteria

Studies were excluded if the same piece of research was reported in more than one article, as they would essentially be duplicates. Conference abstracts were also excluded if an updated report of results (for instance, a full article) was found which contained more information. Articles were also excluded where no results were reported (such as a protocol article).

Literature search strategy

Search terms

The PICOS method [127] was again used in order to develop appropriate search terms (appendix 2). Boolean operators and truncations were used where necessary.

Search methods for identification of studies

Database searches

The following databases were used to search literature with no language or date restrictions:

Ovid MEDLINE® In-Process & Other Non-Indexed Citations and Ovid MEDLINE® 1946 to present*, OvidSP

EMBASE, 1974 to present, OvidSP*

CINAHL Complete, EBSCOhost

*The searches in MEDLINE and EMBASE were run simultaneously due to the OvidSP search engine having access to both databases.

Searching other resources

Grey literature searches were also conducted for both reviews by using the same search terms as for the previous database searches (appendix 3) at www.opengrey.eu.

The bibliographies of the included studies chosen for data extraction were additionally reviewed in order to identify any further potential references.

Appendices

Selection of studies

Results from each search were exported into the reference manager Endnote X7.2.1 and duplicates were removed. There were three key stages to the selection of studies:

Initial screening of titles for relevance to research question. This was carried out simultaneously by two independent researchers R1 and R2.

Abstracts screened against the inclusion criteria for selected titles. This was conducted independently by researchers R1 and R2 simultaneously. The criteria to identify papers for full text retrieval consisted of:

- Research already conducted
- 100% targeted to dementia affected participants
- Community pharmacy team member conducts intervention
- Intervention present
- Community pharmacy setting

Reasons for inclusion and exclusion were documented on a specifically designed form created and managed in Microsoft Excel.

Assessment of full papers for inclusion in the review.

Reasons for inclusion and exclusion at this stage used the same criteria as stage 2 and were also documented in the same method. Like with stage 2, this was conducted independently by R1 and R2 simultaneously.

Any discrepancies between R1 and R2 were resolved by discussion. A Cohens Kappa coefficient was calculated at each stage in order to assess inter-rater agreement.

Data Extraction

Extracted data was recorded in Microsoft Excel using an extraction tool specially designed for the reviews which was based on guidance from the Cochrane Effective Practice and Organisation of Care (EPOC) Review Group Data Collection Checklist [128].

The extraction tool was continuously reviewed and developed by R1 and R2 to ensure that all relevant information was collected.

Assessment of quality

The methodologies were critiqued for bias and quality by the use of an assessment checklist tool which was created by using guidance from the 2009 PRISMA (Preferred Reporting Items for Narrative reviews and Meta-Analysis) checklist tool [130].

All data assessing and grading the quality of the studies was recorded in the assessment template tool developed and managed in Microsoft Excel.

The data was inputted by R1 and periodically reviewed by R2 for accuracy.

Appendix 2. Search strategy used for scoping review

PICOS* criteria	Search term ('.ab,ti.' follows each term where possible)	Step number
Population	Dementia	1
	Alzheimer's	2
	'Creutzfeldt-Jakob'	3
	'vascular dementia'	4
	'lobar degeneration'	5
	Huntington's	6
	'kluver-bucy'	7
	'lewy body disease'	8
	'cognitive impairment'	9
	LBD	10
Intervention	'lewy body disease'	11
	'cognitive impairment'	12
	LBD	13
	Technician	14
	Counter assistant	15
	ACT	16
Outcome	*Unable to search for outcomes as they are currently unknown due to the nature of the study*	
Setting	Community	17
	Pharmacy	18
	'primary care'	19
	Retail	20
	Chemist	21
	'drug store'	22
	1 or 2 or 3 or 4 or 5 or 6	23
	7 or 8 or 9 or 10 or 11 or 12	24
	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	25
	23 and 24 and 25	26

Population, Intervention, Comparison, Outcomes framework

Appendix 3. Search strategy used for narrative review

PICOS* criteria	Step number	Search term ('.ab,ti.' follows each term where possible)
Population	1	dementia
	2	Alzheimer's
	3	creutzfeldt-jakob
	4	'Vascular dementia'
	5	'lobar degeneration'
	6	Huntington's
	7	kluver-bucy
	8	'lewy body disease'
	9	'Cognitive impairment'
	10	LBD
Intervention	11	Dispenser
	12	Pharmacist
	13	Technician
	14	'Counter assistant'
Comparator	*Unable to search for comparators as they are currently unknown due the nature of this review.*	
Outcome	*Unable to search for outcomes are they are currently unknown due the nature of this review.*	
Setting	*To ensure that all settings are included and the breadth of the study optimized, no search terms will be entered in this category.*	
	15	Or/ 1-10
	16	Or/ 11-14
	17	15 AND 16
	18	Remove duplicates

Population, Intervention, Comparison, Outcomes framework

Modified search term phrase for use in OpenGrey

(dementia OR Alzheimer's OR creutzfeldt jakob OR 'vascular degeneration' OR 'lobar degeneration' OR Huntington's OR kluver bucy OR 'lewy body disease' OR 'cognitive impairment' OR LBD) AND (dispenser OR pharmacist OR technician OR 'counter as*')

Appendix 4.1. Details of what was documented on the data extraction form

Data to capture	Subsets of data to capture
Author	Title
Year of research	
Study design	Case study Randomised Retrospective/Prospective/Both Service evaluation Pilot
Country	
Study Setting	
Total Number of settings	
Inclusion Criteria	
Presence of exclusion criteria	Comments
Recruitment method	
Written consent received	Comments
Consent by whom	
Ethics Approval	Ethics approval provided by
Power calculation	
Sample size needed	
Detection of difference details	
Total sample size	(intervention) pre intervention (intervention) post-intervention (Control) pre intervention (Control) post intervention
Key intervention	Brief intervention description
Key intervention conducted by	
Target population	
Is there a follow up?	Details of follow up
Key outcome measures	Humanistic Process Clinical Economical
Key results	Humanistic Process Clinical Economical
Effective methods	Accessibility Patient satisfaction Validated methods Staff training Simple tool Economical Other: Comments
Ineffective elements	Poor communication Selective/self-reporting Self-referral Small area Comments

Appendix 4.2. Details of what information was documented on the quality assessment template

Data to capture	Subset of data to capture
Author	
Cohort representative of sample?	
Objective measures used?	Comments
Validated measurements used?	Comments
Type of sampling method used	Random Convenience Purposive Unknown NA
Was there any blinding?	
Potential for inter-rater reliability bias?	Comments
Potential for intra-rater reliability bias?	Comments
Confounders taken into account?	
Follow up period suitable?	Comments
Are the results reported effectively?	Comments
Was the research funded?	Comments
Could the funding have caused any bias?	Comments
Implications of study for future practice	Positive outcome, promoting service Considers cost Considers patient satisfaction Intervention design is replicable in other settings
Are the results believable?	
Author stated limitations	Other limitations stated by reviewer
Quality of evidence (GRADE)	Study limitations Inconsistency of results Indirectness of evidence Imprecision Reporting bias
Overall quality of paper (GRADE score)	Very low Low Moderate High

Appendix 6. Author and reviewer limitations

Author	Author stated limitations	Reviewer further limitations
Furniss	Only from Manchester so generalisability cannot be assumed. Intervention need further study. Unsure why some recommendations were not followed by GP.	Slight inter-rater reliability bias as initial assessments by pharmacist and psychiatrist followed by 6 nurses for the second and third assessments. No mention of testing their heterogeneity previous to study.
Monette	Open, uncontrolled pilot design. The 1 nursing home may not be representative of other nursing homes. No long-term follow-up. Restricted to those with dementia. Decrease in frequency of disruptive behaviour requires confirmation.	None
Watanabe	Follow-up after peak side effects predicted so may not have been managed. Medication persistence was not followed up in patients who transferred. Results may not be generalisable due to being a university hospital	No long term follow-up. No details on validating / piloting the devised survey.
Child	Dementia may be underreported leading to inaccurate results. Exclusion of some patients and only one PCT means may not be able to generalise. No follow up to see if proposed changes were made. Antipsychotic alternatives were not considered in study.	Short and long term harm/ benefits were not evaluated.
Farrell	none	No long term follow-up of patient. No in depth analysis of cost-effectiveness of this intervention.
Rickles	Voluntary feedback not appropriate method and potential bias introduced. Low voluntary survey completion. 79% referred did not follow up with GP within 60 days.	Self-reporting for the screening may cause selection bias to the study. No cost effectiveness of study conducted so service may not be viable.
Nakamura	Patients and care-givers did not receive any specialised counselling or training	Does not specify any pharmacist training to conduct this intervention. Only 6 men and 21 women patient participants and 2 men and 25 women carer participants. Cohort potentially not representative.
Paquin	No knowledge of admissions to other hospitals regarding 60-day readmittance. Participants not randomized for intervention so control group comprised individuals who could not be contacted. 98% were male. No qualitative aspect for phone calls limited analysis. Not all confounders taken into account (differences in comorbidity, severity of cognitive impairment, caregiver support).	None
Cations	None	Only preliminary data available and limited results reported. Potential bias reporting of outcome measures and is a high recommencement of antipsychotics. 'Organisational culture' not explained.
Collier	None	Only testing in one nursing home. Interesting to test in other teams so see if other factors affect results. No statistical analysis.
Conlon	None	Only testing in one nursing home. Interesting to test in other teams so see if other factors affect results.
D'Souza	Small sample size. Unable to control for unmeasured confounding factors between groups such as behavioural disturbance. Programme evolving in early stages so results may not be representative. Clinical data of insufficient quality and caregiver strain outcomes not evaluated.	Cohort possibly not representative (1.5%, 3.6% respectively female in the COACH and referred groups.)
Frausto	None	May not be able to generalise as 97% were male and only one setting. No validated tool/guide used for reconciliation to reduce inter-rater bias and increase replicability
Hursh	None	Due to being an abstract, limited information on the intervention for replicability and limited results. No statistical significance reported. No demographic information provided. Confounders not mentioned.
Kröger	None	Not enough detail regarding any part of pilot to assess research effectively. No confounders or basic demographic detail listed and no inclusion/exclusion criteria's.
Manrai	None	Only 1 pharmacy and one type of organisational policy used so generalisation cannot be assumed.
Mouchoux	Lack of drug history with patient when admitted to the UCC.	Written in french makes it hard to analyse appropriately. No clinical impact of interventions assessed.
Sakakibara	Not randomised. Psychiatrist placed patients based on personal opinion. Allocation bias potential.	Small sample size and low female ratio (15:4, 10:3).
Stuhec	None	Not enough detail in method and results to make informed decisions. No statistical analysis of results (i.e. relevance of IP decrease from 20 to 6 in 629 patients).

Author	Author stated limitations	Reviewer further limitations
Breslow	Survey items not pilot tested. Self-referral bias. Small sample size limited generalisability. Survey item regarding the recommendation of the service or previous screening not included. Sustainability of service unsure due to ~50% patients willing to pay for service. Complex training was used-perhaps not replicable. Central tendency of Likert Scale	Time point of survey completion. Not made clear in method where completed but if immediately after screening and if pharmacist present, may feel pressured to give positive feedback. Potential inclusion of bias. Use of mean and SD for Likert Scale ordinal data. Not most appropriate descriptive values. (Mode or median more appropriate).
Efjestad	None	Not randomized and no control group. No follow up for long term effects. No clinical outcomes such as falls/ MMSE, ADL assessed for short/ long term benefits.
Maidment	None	Small setting. Use of a niche pharmacist so replicability could be difficult without substantial training. Only one nursing home used so cohort and prescribing habits may differ in other settings.
Patel	None	Very small setting and small sample size. More detail required regarding categorising method. No follow up of the suggestions or clinical outcomes assessed.
Gustafsson	Reviews only conducted in clinics that requested them leading to possible selection bias. No follow-up so unsure if drugs reinstated.	None
Fountain	None	Case study of 1 patient. Economic benefit not considered if a pharmacist was to enter and evaluate every elderly home in this way. Time taken to resolve issues not taken into account.
None	Sample size for audit responses smaller than intended. Cohort not representative as most responses from a high-performing practice. Patient evaluation difficult in dementia. Subjectivity as PCNs self-scored confidence, knowledge and feelings.	None
Anderson	Small sample size. Convenience sampling. Patients asked to fill pillboxes with their own drugs - variability in the difficulty of this task.	None
Setter	Lack of stratification by functional status. High refusal of consent. Lack of follow-up to determine whether screening data became part of medical record or detection of cognitive impairment. Predominantly female and Caucasian cohort,	129 potential patients were not approached based on the nurse case manager's recommendation. Potential recruitment bias.
Sonnett	Potentially misleading information provided by patient in interview if did not want underlying cognitive impairment to be exposed. Medication compliance not performed in detail and potential for self-reporting bias. Medication interactions not reported.	No follow-up of all 'likely impaired' patients for true benefit assessment of service.

Appendix 7. Cross-reference sheet

Name	Ref number	Date

Appendix 8. Data Collection Checklist

Ref	Stage	Age	Gender	Residency	Dysphagia	Smoking Hx	pneumonia	aspiration	Prescribed meds			Dissolve / crush/ half	Vaccine	Comorbidities	Oral health
									Med	Form	Dose				
001	√	√	√			√			√	√			√	√	
002		√	√			√	√		√		√			√	√
…															

Notes

Appendix 9. Letter of access for data collection in hospital

Our Vision
To provide every patient with the care we want for those we love the most

Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Ms Eleanor Reed
School of pharmacy
University of East Anglia,
Norwich Research Park,
Norwich
NR4 7TJ

08/09/2015

Research & Development Office
Level 3 East
Norfolk & Norwich University Hospitals NHS Foundation Trust
Colney Lane
Norwich
NR4 7UY

direct dial: 01603 287806
direct fax: 01603 289800
e-mail: rdoffice@nnuh.nhs.uk
website: www.nnuh.nhs.uk

Dear Ms Eleanor Reed,

Re: (134-09-15) Audit of patients notes retrospectively

Letter of access for research

This letter confirms your right of access to conduct research through Norfolk & Norwich University Hospitals NHS Foundation Trust for the purpose and on the terms and conditions set out below. This right of access commences on 09/09/2015 and ends on 08/09/2018 unless terminated earlier in accordance with the clauses below.

This right of access is conditional upon satisfactory completion of the 'Information Governance Mandatory Training for All Trust Staff'. You must provide a copy of your certificate of completion.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from this NHS organisation. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving permission to conduct the project.

The information supplied about your role in research at Norfolk & Norwich University Hospitals NHS Foundation Trust has been reviewed and you do not require an honorary research contract with this NHS organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out.

This letter of access has been issued in accordance with the Research in the NHS: HR Good Practice Resource Pack. The Algorithm of Research Activity and Pre-engagement Checks states that the following types of research are covered by a letter of access:

- Researcher has opportunity for any form of contact with children in the same Children's Hospital (formerly a specified place) but is not providing healthcare or other types of regulated activity and has no direct bearing on the quality of care.
- Researcher has access to persons in receipt of healthcare services in the course of their normal duties but is not proving health care or other types of regulated activity and has no direct bearing on the quality of care. ('Access' relates to where individuals will have physical, direct contact with patients e.g. observation, qualitative interviews, focus groups).
- Researcher has indirect contact with patients or service users but is not providing healthcare or other types of regulated activity and has not direct bearing on the quality of care (e.g. some types of telephone interview).
- Researcher requires access to identifiable patient data derived from health records,

tissues or organs with no direct bearing on the quality of care.
- Researcher requires access to anonymised patient data derived from health records, tissues or organs only (including by research staff analysing data.
- Researcher is working on NHS premises (e.g. laboratory) only (no access to identifiable data).
- Researcher requires direct contact with staff only but no access to patients (e.g. staff interviews).
- Researcher requires access to identifiable staff data only.
- Researcher requires access to anonymised staff data only.

You are considered to be a legal visitor to Norfolk & Norwich University Hospitals NHS Foundation Trust premises. You are not entitled to any form of payment or access to other benefits provided by this NHS organisation to employees and this letter does not give rise to any other relationship between you and this NHS organisation, in particular that of an employee.

While undertaking research through Norfolk & Norwich University Hospitals NHS Foundation Trust, you will remain accountable to your employer the University of East Anglia but you are required to follow the reasonable instructions of Joanna Ford and Gemma May in this NHS organisation or those given on their behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by this NHS organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with Norfolk & Norwich University Hospitals NHS Foundation Trust policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with Norfolk & Norwich University Hospitals NHS Foundation Trust in discharging its duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on Norfolk & Norwich University Hospitals NHS Foundation Trust premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

If you have a physical or mental health condition or disability which may affect your research role and which might require special adjustments to your role, if you have not already done so, you must notify your employer and the Trust's Workplace Health & Wellbeing Department prior to commencing your research role at the Trust.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice (http://www.dh.gov.uk/assetRoot/04/06/92/54/04069254.pdf) and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that this NHS organisation accepts no responsibility for damage to or loss of personal property.

We may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of this NHS organisation or if you are convicted of any criminal offence.

You must not undertake regulated activity if you are barred from such work. If you are barred from working with adults or children this letter of access is immediately terminated. Your employer will immediately withdraw you from undertaking this or any other regulated activity and you MUST stop undertaking any regulated activity immediately.

Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

Norfolk & Norwich University Hospitals NHS Foundation Trust will not indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in this NHS organisation.

Yours sincerely

LChalkley.

Lisa Chalkley
Research Services Manager

Appendix 10. Initial feedback from ISAC for CPRD project

ISAC EVALUATION OF PROTOCOLS FOR RESEARCH INVOLVING CPRD DATA

FEEDBACK TO APPLICANTS

CONFIDENTIAL	*by e-mail*		
PROTOCOL NO:	16_210		
PROTOCOL TITLE:	The risk factors for pneumonia among those with dementia		
APPLICANT:	Dr George Savva, Senior lecturer, School of health sciences, University of East Anglia, G.Savva@uea.ac.uk		
APPROVED ☐	**APPROVED WITH COMMENTS (resubmission not required)** ☐	**REVISION/ RESUBMISSION REQUESTED** ☒	**REJECTED** ☐

INSTRUCTIONS:

Please include your response/s to the Reviewer's feedback below only if you are required to Revise/ Resubmit your protocol.

Protocols with an outcome of 'Approved' or 'Approved with comments' do not require resubmission to the ISAC.

REVIEWER COMMENTS:

Please address the following comments, revising the protocol as necessary and highlighting all changes:

Lay Summary:

The lay summary needs to focus on the background, purpose and potential importance of the study. Methodological information should not be included.

Technical Summary

The objectives stated in the technical summary mention 'hypothesised risk factors' whereas section C (objectives, specific aims and rationale) emphasizes dysphagia and medicines formulation. The protocol needs to be consistent throughout. Comments regarding the main body of the protocol will necessitate changes to the technical summary.

Objectives, specific aims and rationale

The primary objective is "To determine if dysphagia or particular formulations of medicines are independently associated with an increased likelihood of a patient with dementia being diagnosed with their first episode of pneumonia." This relationship is unlikely to be independent as there is a clear causal association between dysphagia and the prescription of different oral formulations. The background section more logically states that "Our study shall build on these results to firstly determine if a true association between dysphagia and pneumonia exists in a dementia cohort and also whether the association is dependent on the type of formulations prescribed."

Study Population

The start and end of patient follow-up needs to be clearly defined as part of the study population definition. This should include patient registration information (current registration date, transfer out date, death date) as well as practice related dates (UTS date, last collection date). How will change in formulation of medications in 7 days prior to index be defined and applied to both the case and control definitions?

Selection of comparison group(s) or controls

It appears that patients who have a pneumonia diagnosis within 90 days following the dementia diagnosis will be excluded from the cases but not the controls. Rather than starting with case inclusion criteria, it may be easier to first define the study population (patients with dementia) and then describe steps to define the cases.

Data/statistical analysis

The statistical analysis section needs to clearly describe how regression analyses will be used to answer the primary and secondary objectives.

Plan for addressing missing data

There will be a small number of patients with missing IMD quintiles. This is not acknowledged in section N (plan for addressing missing data).

Limitations The limitations section states that cases of pneumonia diagnosed in secondary care will not be in the primary care database. GPs may add this information to the primary care record if they are informed by the hospital and it is considered important for the ongoing care of the patient. It is difficult to know how consistently this will be recorded.	
DATE OF ISAC FEEDBACK:	24/10/2016
DATE OF APPLICANT FEEDBACK:	

Appendix 11. Final Approval of CPRD study from ISAC

ISAC EVALUATION OF PROTOCOLS FOR RESEARCH INVOLVING CPRD DATA

FEEDBACK TO APPLICANTS

CONFIDENTIAL	*by e-mail*		
PROTOCOL NO:	16_210R		
PROTOCOL TITLE:	The risk factors for pneumonia among those with dementia		
APPLICANT:	Dr George Savva, Senior lecturer, School of health sciences, University of East Anglia, G.Savva@uea.ac.uk		
APPROVED ☒	**APPROVED WITH COMMENTS (resubmission not required)** ☐	**REVISION/ RESUBMISSION REQUESTED** ☐	**REJECTED** ☐

INSTRUCTIONS:

Please include your response/s to the Reviewer's feedback below only if you are required to Revise/ Resubmit your protocol.

Protocols with an outcome of 'Approved' or 'Approved with comments' do not require resubmission to the ISAC.

REVIEWER COMMENTS:

This has been approved.

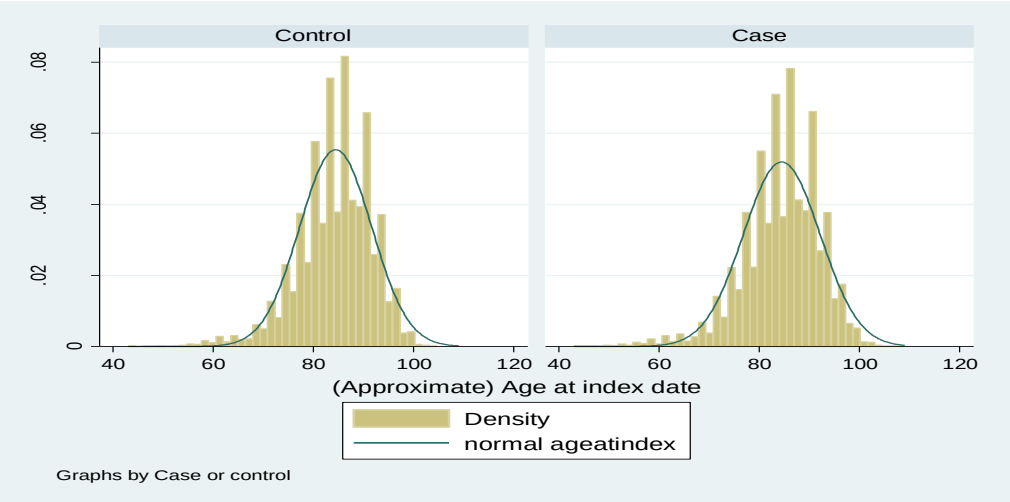
DATE OF ISAC FEEDBACK:	13/01/2017
DATE OF APPLICANT FEEDBACK:	

Appendix 12. Further data analysis for CPRD chapter

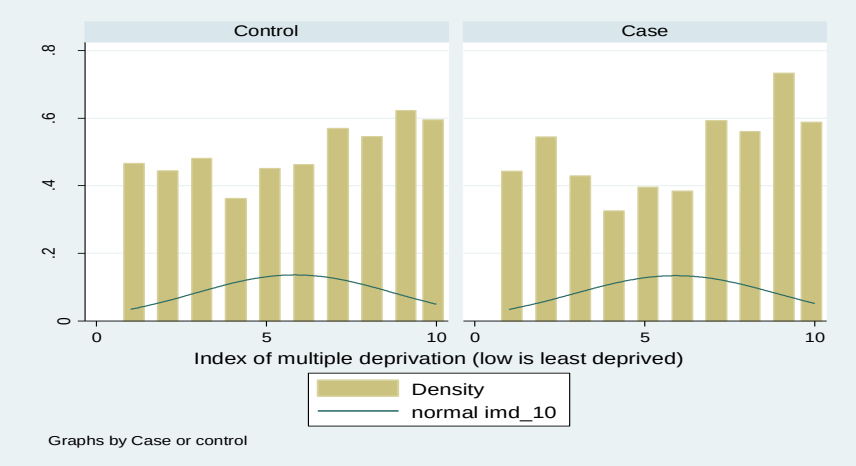
Demographics

Age

The histograms for age showed normal distributions for both cases and controls and therefore mean and standard deviation were recorded.



IMD



The histograms for IMD scores showed a very slight trend in favour of higher IMD scores for both cases and controls.

Influenza diagnoses

Although variables were created for both influenza diagnosis including and excluding the index date, it was decided to use the data including diagnoses from the index date as one theory is that the influenza could still have been one of the factors to lead to pneumonia but was not picked up or diagnosed until the influenza became more severe and became pneumonia.

Individual medicine formulation frequencies

In all medicine groups, the most common formulation used in both controls and cases were oral solids such as tablets and non-oral formulations such as patches or suppositories were the least common (Table A.1).

Table A.1: Frequency and proportions of formulations

Formulation, n (%)	**Control (n=28,671)**	**Case (n=7,259)**
	Donepezil	
Not used	25,638 (89.4)	6,881 (94.8)
Oral solid	2,976 (10.4)	361 (5.0)
Oral Liquid	57 (0.2)	17 (0.23)
Non-Oral	0 (0.0)	0 (0.0)
	Fluoxetine	
Not used	28,208 (98.4)	7,123 (98.1)
Oral solid	409 (1.4)	110 (1.5)
Oral Liquid	54 (0.2)	26 (0.4)
Non-Oral	0 (0.0)	0 (0.0)
	Furosemide	
Not used	25,137 (87.7)	6,190 (85.3)
Oral solid	3,436 (12.0)	1,003 (13.8)
Oral Liquid	98 (0.3)	57 (0.8)
Non-Oral	0 (0.0)	9 (0.1)
	Paracetamol	
Not used	23,430 (81.7)	5,800 (80.0)
Oral solid	4,636 (16.2)	1,066 (14.7)
Oral Liquid	604 (2.1)	370 (5.1)
Non-Oral	1 (0.0)	23 (0.3)
	Risperidone	
Not used	27,950 (97.5)	6,990 (96.3)
Oral solid	660 (2.3)	228 (3.1)
Oral Liquid	61 (0.2)	41 (0.56)
Non-Oral	0 (0.0)	0 (0.0)

Appendix 13. Spearmans Rank results

	pneum	gender	smoke	dysph	copd	stroke	headnec	diabe	heart	acein	AP 1	AP2	fludia	fluvac	pneuvac
pneum	1														
gender	-0.105	1													
	0														
smoke	0.013	-0.154	1												
	0.0134	0													
dysph	0.1325	-0.0151	0.025	1											
	0	0.0041	0												
copd	0.0875	-0.0683	0.102	-0.0013	1										
	0	0	0	0.8085											
stroke	0.0595	-0.0511	-0.0212	0.0414	0.0031	1									
	0	0	0.0001	0	0.5536										
headnec	-0.0002	-0.0162	0.0157	0.0014	0.0046	-0.0007	1								
	0.9745	0.0022	0.0028	0.7888	0.3831	0.8979									
diabe	0.0209	-0.0606	0.1082	0.0097	0.0281	0.0221	-0.0051	1							
	0.0001	0	0	0.0666	0	0	0.3366								
heart	0.0389	-0.0919	0.0874	0.0007	0.0401	0.0472	0.0156	0.0987	1						
	0	0	0	0.8934	0	0	0.0031	0							

	pneum	gender	smoke	dysph	copd	stroke	headnec	diabe	heart	acein	AP 1	AP2	fludia	fluvac	pneuvac
acein	-0.0398	-0.0329	0.1105	-0.0212	0.0341	0.0172	-0.0044	0.1347	0.1091	1					
	0	0	0	0.0001	0	0.0011	0.4064	0	0						
AP 1	0.045	0.0031	-0.0441	0.0072	0.0014	0.0101	-0.008	-0.0068	0.0003	-0.014	1				
	0	0.5611	0	0.1712	0.7943	0.0547	0.1313	0.1998	0.9615	0.0079					
AP 2	0.006	0.0123	0.0438	0.0231	0.0048	-0.023	0.0038	0.0074	0.0004	0.0094	-0.0152	1			
	0.2543	0.0195	0	0	0.3602	0	0.4713	0.1596	0.9386	0.0736	0.0039				
fludiag	0.11	-0.0175	-0.0034	0.0057	0.022	-0.0008	0.009	-0.0025	0.0108	-0.0043	0.0061	0.0006	1		
	0	0.0009	0.5165	0.2811	0	0.8861	0.0893	0.635	0.0406	0.4167	0.2473	0.9156			
fluvac	0.0219	0.0023	0.0605	0.0306	0.0023	0.0201	0.0109	0.0131	0.0361	0.0308	0.0369	0.0498	0.0106	1	
	0	0.662	0	0	0.664	0.0001	0.0386	0.0132	0	0	0	0	0.0449		
pneuvac	0.0025	-0.0803	0.2912	0.0383	0.0736	-0.0468	0.0142	0.1098	0.07	0.1274	-0.0508	0.0572	-0.0045	0.2205	1
	0.6384	0	0	0	0	0	0.0072	0	0	0	0	0	0.3926	0	

Appendix 14. Sensitivity analysis results

Refined models excluding dysphagia

Dysphagia was excluded from models 6-8 to determine the adjusted OR's of formulations within a model not moderated by dysphagia.

Refined model 6: Dysphagia excluded and liquid formulations included

Refined model 6 (Table A.2) included just liquid formulations and the adjusted OR remained similar (2.57) to previously reported in this chapter.

Table A.2 Refined model 6 excluding dysphagia and including liquid formulations

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.57	0.54 – 0.61	<0.001	0.02
COPD*:				
No	1			
Yes	2.08	1.89 – 2.29	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.22	1.14 – 1.30	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.69	0.63 – 0.75	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.52	1.36 – 1.69	<0.001	0.08
Influenza diagnosis#:				
No	1			
Yes	16.82	11.52 – 24.55	<0.001	3.25
Liquid formulation				
No	1			
Yes	2.57	2.28 – 2.91	<0.001	0.16

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; #diagnosis within 1 year of index date but including any diagnoses on index date*

Refined model 7: Dysphagia excluded and solid formulations included

Refined model 7 (Table A.3) includes solid formulations and again the adjusted OR remains similar to previous results in this chapter.

Table A.3. Refined model 7 excluding dysphagia and including solid formulation

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.59	0.56 – 0.62	<0.001	0.02
COPD*:				
No	1			
Yes	2.07	1.89 – 2.27	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.22	1.15 – 1.30	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.70	0.64 – 0.77	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.59	1.43 – 1.76	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	16.55	11.35 – 24.13	<0.001	3.18
Solid formulation				
No	1			
Yes	0.85	0.80 – 0.90	<0.001	0.03

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; #diagnosis within 1 year of index date but including any diagnoses on index date*

Refined model 8: Dysphagia excluded and formulation combination included

Refined model 8 (Table A.4) includes patients that have been prescribed a mixture of solid and liquid formulations of the 5 medicines and likewise to the previous models, no significant changes in adjusted ORs can be seen.

Table A.4. Refined model 8 excluding dysphagia, including formulation combination

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.58	0.55 – 0.62	<0.001	0.02
COPD*:				
No	1			
Yes	2.05	1.87 – 2.25	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.21	1.14 – 1.29	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.68	0.62 – 0.74	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.55	1.39 – 1.73	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	16.54	11.35 – 24.12	<0.001	3.18
Liquid + Solid formulation				
No	1			
Yes	2.62	2.00 – 3.43	<0.001	0.36

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; #diagnosis within 1 year of index date but including any diagnoses on index date*

Determining the independent effect of formulations with presence of dysphagia

To further explore the independent effects of the formulations against dysphagia, the formulation of choice was combined with the dysphagia variable.

Liquid Formulations

Looking at liquid formulations, Table A.5 shows the proportions for those with/ without dysphagia and those with/without liquid formulations prescribed between the groups. Those with pneumonia had a much higher proportion of dysphagia diagnoses but within both groups there was a higher proportion of patients with dysphagia who were not prescribed any liquid formulations of the 5 medicines.

Table A.5. Proportions of patients with/ without dysphagia and also a liquid formulation

	Control (n= 28,671)	**Case (n= 7,259)**
No dysphagia, n (%)	27, 861 (97.2)	6,576 (90.6)
Dysphagia (no liquids prescribed), n (%)	711 (2.5)	578 (8.0)
Dysphagia (liquids prescribed), n (%)	99 (0.4)	105 (1.5)

The unadjusted odds ratios (Table A.6) suggest that as with the previous models, dysphagia strongly increases the chance of getting pneumonia and that liquid formulations do further increase the likeliness and have an independent effect.

Table A.6. Unadjusted odds ratios for dysphagia and liquid formulation variable

Variable	**Unadjusted Odds Ratio**	**95% Confidence Interval**	**P-value**	**Standard Error**
Dysphagia:				
No dysphagia	1			
Dysphagia (no liquids)	3.44	3.06 – 3.87	<0.001	0.21
Dysphagia (liquids)	4.49	3.38 – 5.95	<0.001	0.65

This variable was then added into the refined model to check whether any moderation occurs with the other covariates.

Table A.7 shows that the adjusted OR's for the variable do not alter drastically and are not moderated by the other variables.

Table A.7. Refined model 9. Dysphagia and liquid formulation variable combined

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.59	0.56 – 0.62	<0.001	0.02
COPD*:				
No	1			
Yes	2.10	1.90 – 2.30	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.23	1.15 – 1.31	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.72	0.65 – 0.79	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.58	1.41 – 1.76	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	16.99	11.62 – 24.83	<0.001	3.29
Dysphagia:				
No dysphagia	1			
Dysphagia (no liquids)	3.40	3.02 – 3.83	<0.001	0.21
Dysphagia (liquids)	4.41	3.30 – 5.90	<0.001	0.65
Solid Formulation:				
No	1			
Yes	0.87	0.82 – 0.93	<0.001	0.03

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; #diagnosis within 1 year of index date but including any diagnoses on index date*

Solid Formulations

The distribution of solid formulations amongst those with dysphagia are similar to those seen with liquid formulations (Table A.8). Cases had a higher proportion of patients not prescribed any solid formulations compared to controls and there was a smaller proportion of patients prescribed solids within both groups.

Table A.8. Proportions of patients with/without dysphagia and also a solid formulation

	Control (n= 28,671)	**Case (n= 7,259)**
No dysphagia, n (%)	27,861 (97.2)	6,576 (90.6)
Dysphagia (no solids prescribed), n (%)	607 (2.1)	533 (7.3)
Dysphagia (solids prescribed), n (%)	203 (0.7)	150 (2.1)

The unadjusted OR's (Table A.9) suggest that within those with dysphagia, those who were prescribed solid formulations had a slightly reduced chance of getting pneumonia compared to the controls.

Table A.9. Unadjusted odds ratios for dysphagia and solid formulation variable

Variable	**Unadjusted Odds Ratio**	**95% Confidence Interval**	**P-value**	**Standard Error**
Dysphagia:				
No dysphagia	1			
Dysphagia (no solids)	3.72	3.29 – 4.21	<0.001	0.24
Dysphagia (solids)	3.13	2.52 – 3.89	<0.001	0.35

As with the liquid formulations, the variable was then added into the refined model to check whether any moderation occurs with the other covariates.

Table A.10 shows that the adjusted OR's for the variable do not alter drastically and are not moderated by the other variables. Solid formulations still show a slight protective effect as the OR's reduce from 3.42 to 3.07.

Table A.10. Refined model 10. Dysphagia and liquid formulation variable combined

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.58	0.54 – 0.61	<0.001	0.02
COPD*:				
No	1			
Yes	2.10	1.91 – 2.31	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.23	1.15 – 1.31	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.70	0.64 – 0.77	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.52	1.36 – 1.70	<0.001	0.08
Influenza diagnosis#:				
No	1			
Yes	17.30	11.82 – 25.32	<0.001	3.36
Dysphagia:				
No dysphagia	1			
Dysphagia (no solids)	3.42	3.00 – 3.89	<0.001	0.22
Dysphagia (solids)	3.07	2.45 – 3.84	<0.001	0.35
Liquid Formulation:				
No	1			
Yes	2.27	2.00 – 2.57	<0.001	0.15

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; #diagnosis within 1 year of index date but including any diagnoses on index date*

Solid and Liquid formulation

Associations were also explored for those who were prescribed a combination of liquid and solid formulations.

The trends in distribution were the same as for the solids and liquids on their own and can be seen in Table A.11.

Table A.11. Proportions of patients with/without dysphagia and also both solid and liquid formulations

	Control (n= 28,671)	**Case (n= 7,259)**
No dysphagia, n (%)	27,861 (97.2)	6,576 (90.6)
Dysphagia (no formulation mix), n (%)	802 (2.8)	672 (9.3)
Dysphagia (solid and liquid prescribed), n (%)	8 (0.0)	11 (0.2)

The crude OR's (Table A.12) show that using a combination of formulations within a group of people with dysphagia greatly increases the risk of getting pneumonia compared to those that did not combine formulations. The small numbers involved in this subset have resulted in a higher standard error or 3.23 which should be taken into account.

Table A.12. Unadjusted odds ratios for dysphagia and both solid and liquid formulations variable

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Dysphagia:				
No dysphagia	1			
Dysphagia (no mix)	3.54	3.17 – 3.95	<0.001	0.20
Dysphagia (solid + liquid mix)	6.65	2.57 – 17.21	<0.001	3.23

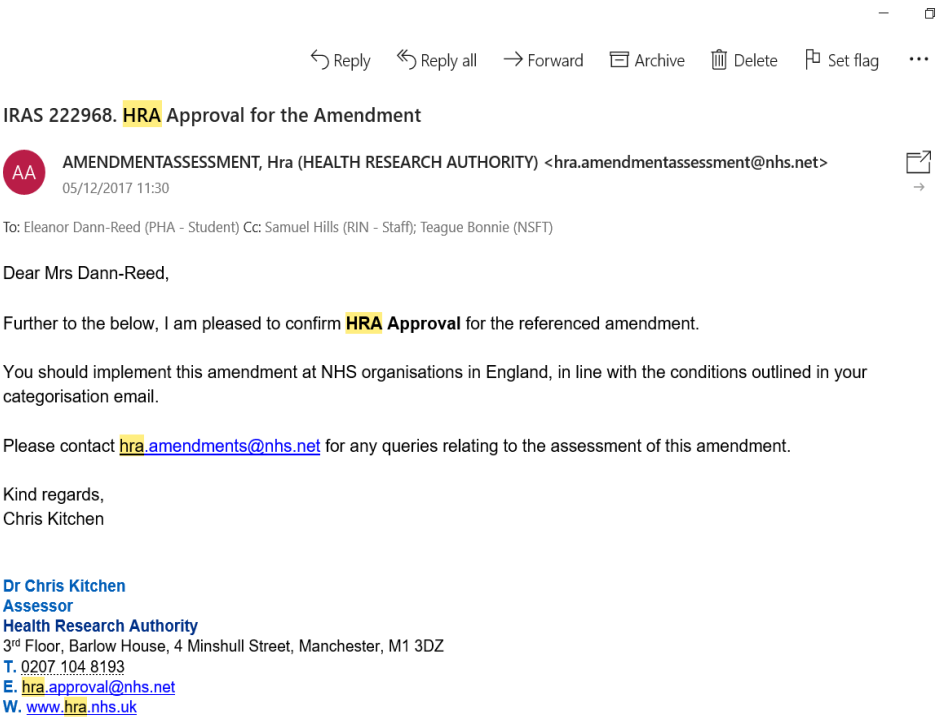
As with previous models in this section, the addition of this variable shows that the results are independent to the other co-variables as the OR's do not become moderated (Table A.13).

Table A.13. Refined model 11. Dysphagia and combination of liquid and solid formulations variable combined

Variable	Adjusted Odds Ratio	95% Confidence Interval	P-value	Standard Error
Gender:				
Male	1			
Female	0.59	0.55 – 0.62	<0.001	0.02
COPD*:				
No	1			
Yes	2.08	1.89 – 2.28	<0.001	0.10
Cardiovascular disease:				
No	1			
Yes	1.22	1.14 – 1.30	<0.001	0.04
Ace Inhibitor:				
No	1			
Yes	0.70	0.64 – 0.77	<0.001	0.03
Antipsychotic (1st):**				
No	1			
Yes	1.56	1.40 – 1.74	<0.001	0.09
Influenza diagnosis#:				
No	1			
Yes	16.98	11.61 – 24.78	<0.001	3.28
Dysphagia:				
No dysphagia	1			
Dysphagia (no mix)	3.54	3.17 – 3.97	<0.001	0.20
Dysphagia (solid + liquid mix))	6.40	2.43 – 16.89	<0.001	3.17

**Chronic Obstructive Pulmonary Disease; **1st generation class of antipsychotic; #diagnosis within 1 year of index date but including any diagnoses on index date*

Appendix 15.1. HRA Approval for amendment on 5.12.17



Reply Reply all Forward Archive Delete Set flag ...

IRAS 222968. HRA Approval for the Amendment

AA **AMENDMENTASSESSMENT, Hra (HEALTH RESEARCH AUTHORITY) <hra.amendmentassessment@nhs.net>**
05/12/2017 11:30

To: Eleanor Dann-Reed (PHA - Student) Cc: Samuel Hills (RIN - Staff); Teague Bonnie (NSFT)

Dear Mrs Dann-Reed,

Further to the below, I am pleased to confirm **HRA Approval** for the referenced amendment.

You should implement this amendment at NHS organisations in England, in line with the conditions outlined in your categorisation email.

Please contact hra.amendments@nhs.net for any queries relating to the assessment of this amendment.

Kind regards,
Chris Kitchen

Dr Chris Kitchen
Assessor
Health Research Authority
3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ
T. 0207 104 8193
E. hra.approval@nhs.net
W. www.hra.nhs.uk

Appendix 15.2. NSFT approval to implement non-substantial amendment to protocol.

RE: IRAS study 222968 request for protocol amendment

RT **Rhodes Tom (NSFT) <Tom.Rhodes@nsft.nhs.uk>**
29/12/2017 11:20

To: Eleanor Dann-Reed (PHA - Student)

Dear Elly,

Study title: Living with Dementia and managing medicines
IRAS Project ID: 222968
R&D approval number: RD #17 222968
Amendment number and date: NSA1, 30/11/17

I am writing to confirm that this amendment has been reviewed at the Norfolk and Suffolk NHS Foundation Trust and can be implemented at this site under the existing HRA and R&D permission.

Please note that you may only implement changes that are outlined in the amendment notice or letter.

If other Trusts are involved in your project, please ensure that the R&D office for each Trust is aware of this amendment before implementing the changes at those sites.

Kind regards,
Tom

Tom Rhodes – Senior Research Facilitator
Norfolk and Suffolk NHS Foundation Trust
Research and Development, The Knowledge Centre
Hellesdon Hospital, Drayton High Road, Norwich, NR6 5BE

Appendix 16. Recruitment checklist

Norfolk and Suffolk NHS
NHS Foundation Trust

University of East Anglia

Living with dementia and managing medicines

Recruitment checklist

Please don't forget to check each patient prior to arranging a medicine follow-up meeting to see if they are eligible to take part in our research study!

- Do they have a diagnosis of **dementia**? ☐
- If **yes**, is it classed as **mild** or **moderate**? ☐
- Do they **have capacity** based on their consent for disclosure form? ☐
- Have they ticked **YES** for information to be shared 'for research purposes' on their consent for disclosure form? ☐
- Do they live **at home** in the community? ☐
- If they live with or have a carer, are they **UNPAID**? ☐

For eligible participants please request their consent for Elly to join you at your medicine follow up visit, to explain their potential interest in taking part in her study by asking the following paragraph during your contact with them to arrange the meeting.

[If they are a patient living **independently**]

"A small research study at the University of East Anglia is seeking patients to take part in a study to be observed by a research pharmacist for a short period of time to find out more about possible ways to improve how we can manage medicines for patients like you. Would you be interested in finding out more about this study and what it would be like to take part?"

[If they are a patient with an **informal carer**]

"A small research study at the University of East Anglia is seeking patients with dementia and their carers to take part in a study to be observed by a research pharmacist for a short period of time to find out more about possible ways to improve how we can manage medicines for patients like you. Would you be interested in finding out more about this study and what it would be like to take part?"

If say YES – please explain how Elly will join you at your next appointment to meet them in person and give them more information. Please also explain how they are able to stop taking part in this study at any time.

Please now complete a confidential summary sheet and then email Elly to let her know you have a new appointment.

Elly's email: e.reed@uea.ac.uk

THANK YOU

University of East Anglia

Norfolk and Suffolk NHS
NHS Foundation Trust

Appendix 17. Confidential summary sheet

Living with dementia and managing medicines

Potential participant/ participant summary sheet

CONFIDENTIAL

First name	
Surname	
First name (if dyad) (Please write N/A if not)	
Surname (if dyad) (Please write N/A if not)	
Address	
Contact number	
Medicine List	
Study Reference number	
Other information to be recorded	

To be stored in secure area of the Julian Hospital with original consent forms and **destroyed 2 months after the study has finished.**

Appendix 18. Cover letter

IRAS: 222968 Cover letter V1 31.05.17

Norfolk and Suffolk NHS
NHS Foundation Trust

Mrs Elly Dann-Reed

Medicine Management Group
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ
March 2017
Tel: 01603 591973
Email: e.reed@uea.ac.uk

Dear [handwritten participants name],

You are invited to take part in the following research study to be carried out by Elly Dann-Reed from the University of East Anglia:

Living with dementia and managing medicines

We are giving you an information sheet (yellow) to people who may be interested in taking part in this study to explain what taking part would involve. Elly will talk to you face to face to explain why this study is important. After Elly has talked to you please read this information in your own time.

If you decide you would like to take part in this study please read and initial the enclosed consent form (green) including a daytime contact telephone number **within 7 days of meeting Elly face to face** using the self-addressed envelope.

Elly will then contact you to arrange a date and time that suits you when she can visit.

If you **do not wish** to take part in this study then you do not need to do anything. If we do not hear from you within 7 days, we shall give you a quick call just to check that you have had a chance to read this information.

Thank you for taking the time to read this.
Kind regards,

[Sig]
Elly Dann-Reed
Research Pharmacist

1

Appendix 19. Participant Information Sheet: PWD living alone

Norfolk and Suffolk NHS
NHS Foundation Trust

UEA
University of East Anglia

Participant Information Sheet: Participant living alone with dementia

Living with dementia and managing medicines

Invitation

You are invited to take part in a research study.
Before you decide to take part, you need to understand why the research is being done and what it will involve for you, if you take part. Please take some time to read through this information.

What is the purpose of the study?

The aim of this study is to find out how people with memory problems manage their medicines at home. This may include how medicines are ordered, collected, stored, what happens when you take them and how you get the right medicines prescribed. We also aim to find out how (if at all) your regular doctor, community nurse or pharmacist could support people with mild-moderate dementia better in the future.

What will taking part in this study involve for me?

Elly is the researcher who you met during your new dementia medicine follow up meeting. If you decide to post back your consent form expressing your wishes to take part in this study, Elly will give you a telephone call using the number you provided. During this phone call, she will arrange with you a good time to visit you at home and a maximum length of time (up to 3 hours) to spend with you that you are comfortable with. We hope, where possible, to arrive at your home at least one hour before you usually take some of you medicines but we will discuss this with you on the telephone and will only arrive at a time that is suitable for you.

About 1 week before the date you agreed for Elly to come and visit you, you will receive a letter to remind you. The day before the date you agreed for Elly to visit you, she will phone you to remind you about this and to check that you are still happy to go ahead with her visit.

When Elly arrives, she will watch you do whatever you normally do on that day and during that time but she will not follow you into any private areas such as the bathroom or your bedroom. Elly will talk with you to find out a bit more about what she notices during her time with you. Elly will audio-record your conversation with her, to be sure her notes about her visit with you are accurate.

During her time with you, Elly may also take up to 3 photographs of things in your home that relate to your medicines. This is because sometimes a picture can help show practical arrangements more clearly than words. These photos will not include images of you or any text which could identify you.

Elly will also make some notes throughout this time. She will use the recordings, notes and any photographs taken to help ensure she has accurate details of her time with you to analyse for this research.

Elly will only visit you at home up to the length of time agreed between you and Elly but she may leave in a shorter amount of time if she feels that all of the required information has been collected.

Elly may see sensitive information such as your medicines and any directions about how you should use them.

Any information about you which Elly collects will remain confidential and you will not be identifiable in any research reports or findings that are shared.

However, if any signs of harm or serious safety concerns to you or anyone else are observed, she may share these with a relevant healthcare professional or organisation.

You will not be expected to provide refreshments for Elly whilst she is with you.

Why have I been chosen?

You have been chosen because the community mental health nurse that has arranged this follow up appointment with you has noticed that you have a recent diagnosis of mild-moderate dementia and live at home without someone who gets paid to look after you. We hope to be able to help people with similar circumstances to you in the future.

Do I have to take part?

No. It is up to you whether or not you take part. If you choose to take part in the study, please sign the enclosed green consent form and post it back to Elly. Even after you have signed a consent form, you are still **free to stop taking part in the study at any time and without giving a reason. However, if you stop taking part in the study during the visit, any data collected up to the point to when you wished to stop will be included in the research analysis unless you tell Elly that you do not want any of the data collected to be used in any way.**

If you choose not to take part, this will not affect your rights in any way. Any care that you are currently receiving will also not be affected.
If you want more independent information or advice about your rights about being involved in this research study, you can get this by contacting Professor David Wright who is a supervisor for this study.

His contact details are:

Professor David Wright, School of Pharmacy at the University of East Anglia.
Telephone: 01603 592042 Email D.J.Wright@uea.ac.uk

What are the possible benefits of taking part?

This study will give you a rare opportunity to show a pharmacist how you manage your medicines first hand and express your views about how your community pharmacy, doctor's surgery or community nurses are supporting you and what could be improved.

What are the possible disadvantages of taking part?

Elly is mindful that some participants may become distressed or anxious during her visits due to a stranger being in their home. If Elly sees any signs of you feeling uncomfortable, during her visit, she will stop audio-recording and check with you if you are happy to go ahead and remind you that you can stop the study at any time.

If you feel uncomfortable at any time during the process or wish for certain things to not be photographed or written down, please let Elly know and she will act on your concerns.

What if there is a problem?

If you have any complaints about what happens to you during the study or any concerns about possible harm to you, these will be addressed.

If you have any concerns please contact Professor David Wright, who is a senior member of staff within the School of Pharmacy at the University of East Anglia, and who is a supervisor for this study, on 01603 592042 or email D.J.Wright@uea.ac.uk.

What happens after the project comes to an end?

After identifying details (such as your name and address) have been removed, the data will be analysed by Elly and the supervisory team. Elly will then publish some of this non-identifying data in her PhD thesis and may present it to the Norfolk and Suffolk NHS Foundation trust, dementia cafes and academic or professional conferences.

Will my taking part in the study be kept confidential?

Yes.

Although data may be accessed for auditing purposes by the NHS to make sure that this study is being carried out properly.

All your personal information and your consent form will be stored by Elly and the NHS in a secured area of The Julian Hospital based on Bowthorpe Road,

Norwich. These documents will only be viewed by Elly and NHS staff. All confidential documents will be destroyed 2 months after the end of this study.

Elly will take out details that identify you from information collected for the study. She will be analysing information with support from her supervisory team but the supervisor team will only see information with your identifying details removed. This information will be stored on a password-protected computer, will only be used for Elly's research and is kept within a securely-locked office at the University of East Anglia. Any non-identifiable research data will be stored for 10 years from the end of the study period.

What will happen to the results of the research?

The study results will be about how medicines are managed in the homes of people with mild to moderate dementia and how community pharmacies and other local healthcare teams could support them better. The study findings will be written up as part of a doctoral thesis. A copy of the thesis will be kept in the library of the University of East Anglia. The results may also be published in an academic or professional journal. These will be used to add to scientific knowledge in this area and to share the results with other health professionals.

Who is organising and funding the research?

The research is organised and funded through the School of Pharmacy at the University of East Anglia and Rosemont Pharmaceuticals. The information we collect is being used for Elly's postgraduate research degree. A team of experienced researchers is supervising the research.

Contact details:

If you would like further information about this study or have any further questions, you can contact Elly Dann-Reed by:

Telephone: 01603 591996

Email: e.reed@uea.ac.uk

Post: Medicines Management Research Group, School of Pharmacy, University of East Anglia, and Norwich, NR4 7TJ.

Thank you for taking the time to consider being involved in this project

Appendix 20. Participant Information Sheet: PWD living with carer

Norfolk and Suffolk NHS
NHS Foundation Trust

UEA
University of East Anglia

Participant Information Sheet: Participant with dementia, living with a carer

Living with dementia and managing medicines

Invitation

You and your carer are invited to take part in a research study.
Before you decide to take part, you need to understand why the research is being done and what it will involve for you, if you take part. Please take some time to read through this information.

What is the purpose of the study?

The aim of this study is to find out how people with memory problems manage their medicines at home. This may include how medicines are ordered, collected, stored, what happens when you take them and how you get the right medicines prescribed. We also aim to find out how (if at all) your regular doctor, community nurse or pharmacist could support people with mild-moderate dementia better in the future.

What will taking part in this study involve for me?

Elly is the researcher who you met during your new dementia medicine follow up meeting. If you and your carer decide to post back your consent forms expressing your wishes to take part in this study, Elly will give you a telephone call using the number you provided. During this phone call, she will arrange with you and your carer a good time to visit you both at home. She will also arrange and a maximum length of time (up to 3 hours) to spend with you both that you are comfortable with. We hope, where possible, to arrive at your home at least one hour before you usually take some of you medicines but we will discuss this with you on the telephone and will only arrive at a time that is suitable for both of you.

About 1 week before the date you agreed for Elly to come and visit you, you will receive a letter to remind you. The day before the date you agreed for Elly to visit you, she will phone you to remind you about this and to check that you are both still happy to go ahead with her visit.

When Elly arrives, she will watch you and your carer do whatever you normally do on that day and during that time but she will not follow you into any private areas such as the bathroom or your bedroom. Elly will talk with you and your carer to find out a bit more about what she notices during her time with you. Elly will audio-record your conversation with her, to be sure her notes about her visit with you are accurate.

During her time with you, Elly may also take up to 3 photographs of things in your home that relate to your medicines. This is because sometimes a picture can help show practical arrangements more clearly than words. These photos will not include images of you or any text which could identify you or your carer.

Elly will also make some notes throughout this time. She will use the recordings, notes and any photographs taken to help ensure she has accurate details of her time with you and your carer to analyse for this research.

Elly will only visit you at home up to the length of time agreed between you and Elly but she may leave in a shorter amount of time if she feels that all of the required information has been collected.

Elly may see sensitive information such as your medicines and any directions about how you should use them.

Any information about you which Elly collects will remain confidential and you will not be identifiable in any research reports or findings that are shared.

However, if any signs of harm or serious safety concerns to you or anyone else are observed, she may share these with a relevant healthcare professional or organisation.

You will not be expected to provide refreshments for Elly whilst she is with you.

Why have I been chosen?

You have been chosen because the community mental health nurse that has arranged this follow up appointment with you has noticed that you have a recent diagnosis of mild-moderate dementia and live at home without someone who gets paid to look after you. We hope to be able to help people with similar circumstances to you in the future.

Do I have to take part?

No. It is up to you whether or not you take part. If you choose to take part in the study, please sign the enclosed green consent form titled **'Consent Form for a participant living with dementia with a carer'** and post it back to Elly along with your carer's consent form. The study will only go ahead if Elly receives consent forms from both you and your carer.

Even after you have signed a consent form, you and your carer are still **free to stop taking part in the study at any time and without giving a reason. However, if you stop taking part in the study during the visit, any data collected up to the point to when you wished to stop will be included in the research analysis unless you tell Elly that you do not want any of the data collected to be used in any way.**

If you or your carer choose not to take part, this will not affect your rights in any way. Any care that you are currently receiving will also not be affected.

If you want more independent information or advice about your rights about being involved in this research study, you can get this by contacting Professor David Wright who is a supervisor for this study.

His contact details are:

Professor David Wright, School of Pharmacy at the University of East Anglia.
Telephone: 01603 592042 Email D.J.Wright@uea.ac.uk

What are the possible benefits of taking part?

This study will give you and your carer a rare opportunity to show a pharmacist how you manage your medicines first hand and express your views about how your community pharmacy, doctor's surgeries or community nurses are supporting you and what could be improved.

What are the possible disadvantages of taking part?

Elly is mindful that some participants may become distressed or anxious during her visits due to a stranger being in their home. If Elly sees any signs of you or your carer feeling uncomfortable, during her visit, she will stop audio-recording and check with you if you are happy to go ahead and remind you that you or your carer can stop the study at any time.

If either of you feel uncomfortable at any time during the process or wish for certain things to not be photographed or written down, please let Elly know and she will act on your concerns.

What if there is a problem?

If you or your carer have any complaints about anything that happens during the study or any concerns about possible harm, these will be addressed.

If you have any concerns please contact Professor David Wright, who is a senior member of staff within the School of Pharmacy at the University of East Anglia, and who is a supervisor for this study, on 01603 592042 or email D.J.Wright@uea.ac.uk.

What happens after the project comes to an end?

After identifying details (such as your name and address) have been removed, the data will be analysed by Elly and the supervisory team. Elly will then publish some of this non-identifying data in her PhD thesis and may present it to the Norfolk and Suffolk NHS Foundation trust, dementia cafes and academic or professional conferences.

Will my taking part in the study be kept confidential?

Yes.

Although data may be accessed for auditing purposes by the NHS to make sure that this study is being carried out properly.

All your personal information and your consent form will be stored by Elly and the NHS in a secured area of The Julian Hospital based on Bowthorpe Road, Norwich. These documents will only be viewed by Elly and NHS staff. All confidential documents will be destroyed 2 months after the end of this study.

Elly will take out details that identify you from information collected for the study. She will be analysing information with support from her supervisory team but the supervisory team will only see information with your identifying details removed. This information will be stored on a password-protected computer, will only be used for Elly's research and is kept within a securely-locked office at the University of East Anglia. Any non-identifiable research data will be stored for 10 years from the end of the study period.

What will happen to the results of the research?

The study results will be about how medicines are managed in the homes of people with mild to moderate dementia and how community pharmacies and other local healthcare teams could support them better. The study findings will be written up as part of a doctoral thesis. A copy of the thesis will be kept in the library of the University of East Anglia. The results may also be published in an academic or professional journal. These will be used to add to scientific knowledge in this area and to share the results with other health professionals.

Who is organising and funding the research?

The research is organised and funded through the School of Pharmacy at the University of East Anglia and Rosemont Pharmaceuticals. The information we collect is being used for Elly's postgraduate research degree. A team of experienced researchers is supervising the research.

Contact details:

If you would like further information about this study or have any further questions, you can contact Elly Dann-Reed by:

Telephone: 01603 591996

Email: e.reed@uea.ac.uk

Post: Medicines Management Research Group, School of Pharmacy, University of East Anglia, and Norwich, NR4 7TJ.

Thank you for taking the time to consider being involved in this project

Appendix 21. Participant Information Sheet: Carer

Norfolk and Suffolk NHS
NHS Foundation Trust

UEA
University of East Anglia

Participant Information Sheet: Carer for participant living with dementia

Living with dementia and managing medicines

Invitation

You and the person you care for are invited to take part in a research study. Before you decide to take part, you need to understand why the research is being done and what it will involve for you, if you take part. Please take some time to read through this information.

What is the purpose of the study?

The aim of this study is to find out how people with memory problems manage their medicines at home. This may include how medicines are ordered, collected, stored, what happens when you take them and how you get the right medicines prescribed. We also aim to find out how (if at all) your regular doctor, community nurse or pharmacist could support people with mild-moderate dementia better in the future.

What will taking part in this study involve for me?

Elly is the researcher who you met during the follow up meeting about the new dementia medicine given to the person you care for. If both you and the person you care for decide to post back your consent forms expressing your wishes to take part in this study, Elly will give you a telephone call using the number you provided. During this phone call, she will arrange with you and the person you care for a good time to visit you both at home. She will also arrange a maximum length of time (up to 3 hours) to spend with you both that you are comfortable with. We hope, where possible, to arrive at the home of the person you care for at least one hour before they usually take some of their medicines but we will discuss this with you on the telephone and will only arrive at a time that is suitable for the both of you.

About 1 week before the date you agreed for Elly to come and visit you, you will receive a letter to remind you. The day before the date you agreed for Elly to visit you, she will phone you to remind you about this and to check that you are still happy to go ahead with her visit.

When Elly arrives, she will watch you and the person you care for do whatever you normally do on that day and during that time but she will not follow you into any private areas such as the bathroom or your bedroom. Elly will talk with you and the person you care for to find out a bit more about what she notices during her time with you. Elly will audio-record your conversation with her, to be sure her notes about her visit with you are accurate.

During her time with you, Elly may also take up to 3 photographs of things in your home that relate to the medicines of the person you care for. This is because sometimes a picture can help show practical arrangements more clearly than words. These photos will not include images of you or any text which could identify you or the person you care for.

Elly will also make some notes throughout this time. She will use the recordings, notes and any photographs taken to help ensure she has accurate details of her time with you to analyse for this research.

Elly will only visit you at home up to the length of time agreed between you and Elly but she may leave in a shorter amount of time if she feels that all of the required information has been collected.

Elly may see sensitive information such as your medicines and any directions about how you should use them.

Any information about you which Elly collects will remain confidential and you will not be identifiable in any research reports or findings that are shared.

However, if any signs of harm or serious safety concerns to you or anyone else are observed, she may share these with a relevant healthcare professional or organisation.

You will not be expected to provide refreshments for Elly whilst she is with you.

Why have I been chosen?

You have been chosen because you are an unpaid carer for someone that the community mental health nurse has noticed lives at home with a recent diagnosis of mild-moderate dementia. We hope to be able to help people with similar circumstances to you in the future.

Do I have to take part?

No. It is up to you whether or not you take part. If you choose to take part in the study, please sign the enclosed green consent form titled **'Consent Form for a carer participant'** and post it back to Elly along with the consent form signed by the person you care for. The study will only go ahead when Elly receives consent forms from both you and the person you care for.
Even after you have signed a consent form, you and the person you care for are still **free to stop taking part in the study at any time and without giving a reason. However, if you stop taking part in the study during the visit, any data collected up to the point to when you wished to stop will be included in the research analysis unless you tell Elly that you do not want any of the data collected to be used in any way.**

If you or the person you care for choose not to take part, this will not affect your rights in any way. Any care that you are currently receiving will also not be affected.
If you want more independent information or advice about your rights about being involved in this research study, you can get this by contacting Professor David Wright who is a supervisor for this study.

His contact details are:

Professor David Wright, School of Pharmacy at the University of East Anglia.
Telephone: 01603 592042 Email D.J.Wright@uea.ac.uk

What are the possible benefits of taking part?

This study will give you a rare opportunity to show a pharmacist how you and the person you care for manage their medicines first hand and express your views about how your community pharmacy, doctor's surgery or community nurses are supporting you and what could be improved.

What are the possible disadvantages of taking part?

Elly is mindful that some participants may become distressed or anxious during her visits due to a stranger being in their home. If Elly sees any signs of you or the person you care for feeling uncomfortable, during her visit, she will stop audio-recording and check with you if you are happy to go ahead and remind you that you or the person you care for can stop the study at any time.
If either of you feel uncomfortable at any time during the process or wish for certain things to not be photographed or written down, please let Elly know and she will act on your concerns.

What if there is a problem?

If you have any complaints about what happens to you during the study or any concerns about possible harm to you, these will be addressed.
If you have any concerns please contact Professor David Wright, who is a senior member of staff within the School of Pharmacy at the University of East Anglia, and who is a supervisor for this study, on 01603 592042 or email D.J.Wright@uea.ac.uk.

What happens after the project comes to an end?

After identifying details (such as your name and address) have been removed, the data will be analysed by Elly and the supervisory team. Elly will then publish some of this non-identifying data in her PhD thesis and may present it

to the Norfolk and Suffolk NHS Foundation trust, dementia cafes and academic or professional conferences.

Will my taking part in the study be kept confidential?

Yes.

Although data may be accessed for auditing purposes by the NHS to make sure that this study is being carried out properly.

All your personal information and your consent form will be stored by Elly and the NHS in a secured area of The Julian Hospital based on Bowthorpe Road, Norwich. These documents will only be viewed by Elly and NHS staff. All confidential documents will be destroyed 2 months after the end of this study.

Elly will take out details that identify you from information collected for the study. She will be analysing information with support from her supervisory team but the supervisor team will only see information with your identifying details removed. This information will be stored on a password-protected computer, will only be used for Elly's research and is kept within a securely-locked office at the University of East Anglia. Any non-identifiable research data will be stored for 10 years from the end of the study period.

What will happen to the results of the research?

The study results will be about how medicines are managed in the homes of people with mild to moderate dementia and how community pharmacies and other local healthcare teams could support them better. The study findings will be written up as part of a doctoral thesis. A copy of the thesis will be kept in the library of the University of East Anglia. The results may also be published in an academic or professional journal. These will be used to add to scientific knowledge in this area and to share the results with other health professionals.

Who is organising and funding the research?

The research is organised and funded through the School of Pharmacy at the University of East Anglia and Rosemont Pharmaceuticals. The information we collect is being used for Elly's postgraduate research degree. A team of experienced researchers is supervising the research.

Contact details:

If you would like further information about this study or have any further questions, you can contact Elly Dann-Reed by:

Telephone: 01603 591996

Email: e.reed@uea.ac.uk

Post: Medicines Management Research Group, School of Pharmacy, University of East Anglia, and Norwich, NR4 7TJ.

Thank you for taking the time to consider being involved in this project

Appendix 22. Consent form: PWD living alone

Norfolk and Suffolk NHS
NHS Foundation Trust

UEA
University of East Anglia

Living with dementia and managing medicines

Consent Form for a participant living with dementia

Please initial the box for each statement that you agree with.

I have had the opportunity to consider the information provided in the information sheet, ask any questions and to have these answered	☐
I understand that if the researcher observes something which could likely lead to harm, she may need to speak to somebody that could help	☐
I understand that my taking part is voluntary and that I am free to stop taking part at any time and without giving any reasons	☐
I agree to be observed in my home during a time when I usually takes my regular medicines	☐
I agree for the observation to be audio-recorded	☐
I agree for the researcher to have access to my medical information and to record any relevant anonymised information	☐
I am happy for up to 3 photographs to be taken during the observation which will be unidentifiable to me	☐

Please turn over to complete the form.

I agree to take part in this observation study ☐

I understand that if I stop taking part during the study, any anonymous data already collected will still be used unless I tell Elly otherwise ☐

I understand that only Elly will have access to confidential information and that it will be stored in a secure place for 2 months ☐

I understand that the research data may be accessed by the NHS for auditing purposes to check that the study is being carried out as expected ☐

Name of **participant living with dementia**:

Signature:

Date:

Contact telephone number:

REF:

Name of **researcher (please leave this blank)**:

Signature:
Date:

Thank you for completing this form.

Please post this form back to Elly, using the stamped addressed envelope provided in your research pack. We will send you a copy of this consent form back to you with your visit reminder letter.

Appendix 23. Consent form: PWD living with carer

Norfolk and Suffolk NHS
NHS Foundation Trust

UEA
University of East Anglia

Living with dementia and managing medicines

Consent Form for a participant living with dementia with a carer

Please initial the box for each statement that you agree with.

I have had the opportunity to consider the information provided in the information sheet, ask any questions and to have these answered	☐
I understand that if the researcher observes something which could likely lead to harm, she may need to speak to somebody that could help	☐
I understand that my taking part is voluntary and that I am free to stop taking part at any time and without giving any reasons	☐
I agree for my carer and I to be observed in my home, during a time when I usually takes my regular medicines	☐
I agree for the observation to be audio-recorded	☐
I agree for the researcher to have access to my medical information and to record any relevant anonymised information	☐
I am happy for up to 3 photographs to be taken during the observation which will be unidentifiable to me	☐

Please turn over to complete the form.

I agree to take part in this observation study with my carer present ☐

I understand that if I or my carer stop taking part during the study, any anonymous data already collected will still be used unless I tell Elly otherwise ☐

I understand that only Elly will have access to confidential information and that it will be stored in a secure place for 2 months ☐

I understand that the research data may be accessed by the NHS for auditing purposes to check that the study is being carried out as expected ☐

Name of **participant living with dementia**:

Signature:

Date:

REF:

Contact telephone number:

Name of **researcher (please leave this blank)**:

Signature:
Date:

Thank you for completing this form.

Please post this form back to Elly, using the stamped addressed envelope provided in your research pack. We will send you a copy of this consent form back to you with your visit reminder letter.

Appendix 24. Consent form: Carer

IRAS: 222968 Consent form: Dyad- Carer V2 07.08.17

Norfolk and Suffolk NHS
NHS Foundation Trust

UEA
University of East Anglia

Living with dementia and managing medicines

Consent Form for a carer participant

Please initial the box for each statement that you agree with.

I have had the opportunity to consider the information provided in the information sheet, ask any questions and to have these answered	☐
I understand that if the researcher observes something which could likely lead to harm, she may need to speak to somebody that could help	☐
I understand that my taking part is voluntary and that I am free to stop taking part at any time and without giving any reasons	☐
I agree to be observed in the home of the person I care for during a time when that person usually takes their regular medicines	☐
I agree for the observation to be audio-recorded	☐
I agree for the researcher to have access to my medical information and to record any relevant anonymised information	☐
I am happy for up to 3 photographs to be taken during the observation which will be unidentifiable to me	☐

Please turn over to complete the form.

1

I agree to take part in this observation study with the person that I care for ☐

I understand that if I, or the person that I care for stops taking part during the study, any anonymous data already collected will still be included in the data analysis unless I tell Elly otherwise ☐

I understand that my personal information will be kept confidential and will be destroyed 2 months after the end of the study ☐

I understand that the data collected in this study may be accessed by the NHS trust for auditing purposes to check that the study is being carried out as expected ☐

Name of **participant (carer):**

REF:

Signature:

Date:

Contact telephone number:

Name of **researcher (please leave this blank):**

Signature:
Date:

Thank you for completing this form.

Please post this form back to Elly, using the stamped addressed envelope provided in your research pack. We will send you a copy of this consent form back to you with your visit reminder letter.

Appendix 25. Reminder letter: PWD living alone

IRAS: 222968 Reminder Letter: independent V1 31.05.17

Mrs Elly Dann-Reed

Medicine Management Group
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ
March 2017
Tel: 01603 591973
Email: e.reed@uea.ac.uk

Dear [participants name],

My name is Elly and I spoke to you on the phone on [x/x/date] to arrange what day and time would be best for me to come and visit you at your home and spend an agreed amount of time with you to learn more about how you manage your medicines as part of a research project.

This is just a reminder letter to let you know that I will be **visiting you** on:

[Insert date in Wednesday 20th March format]

At: [time]

Please let me know as soon as possible if something changes and this date or time is not suitable for you anymore.

Please do not feel that you have to take part in this study. You are free to change your mind and stop taking part at any time. Just let us know.

I will give you a final telephone call the day before I am due to visit to remind you that I am coming and to check that you are still happy for me to spend some time with you.

As always, please feel free to give me a call at any time if you have any further questions or concerns.

I have also included a copy of your consent form that you kindly completed for your records.

I look forward to visiting you,

Kind Regards,

[sig]

Elly Dann-Reed
Research Pharmacist

1

Appendix 26. Reminder lettter: PWD living with carer

IRAS: 222968 Reminder Letter: dyad V1 31.05.17

Mrs Elly Dann-Reed

Medicine Management Group
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ
March 2017
Tel: 01603 591973
Email: e.reed@uea.ac.uk

Dear [participants name],

My name is Elly and I spoke to you on the phone on [x/x/date] to arrange what day and time would be best for me to come and visit you both at your home and spend an agreed amount of time with you to learn more about how you manage the medicines of the person living with dementia as part of a research project.

This is just a reminder letter to let you know that I will be **visiting you** on:

[Insert date in Wednesday 20th March format]

At: [time]

Please let me know as soon as possible if something changes and this date or time is not suitable for you anymore.

Please do not feel that you have to take part in this study. You are free to change your mind and stop taking part at any time. Just let us know.

I will give you a final telephone call the day before I am due to visit to remind you that I am coming and to check that you are both still happy for me to spend some time with you.

As always, please feel free to give me a call at any time if you have any further questions or concerns.

I have also included a copy of your consent form that you kindly completed for your records.

I look forward to visiting you,

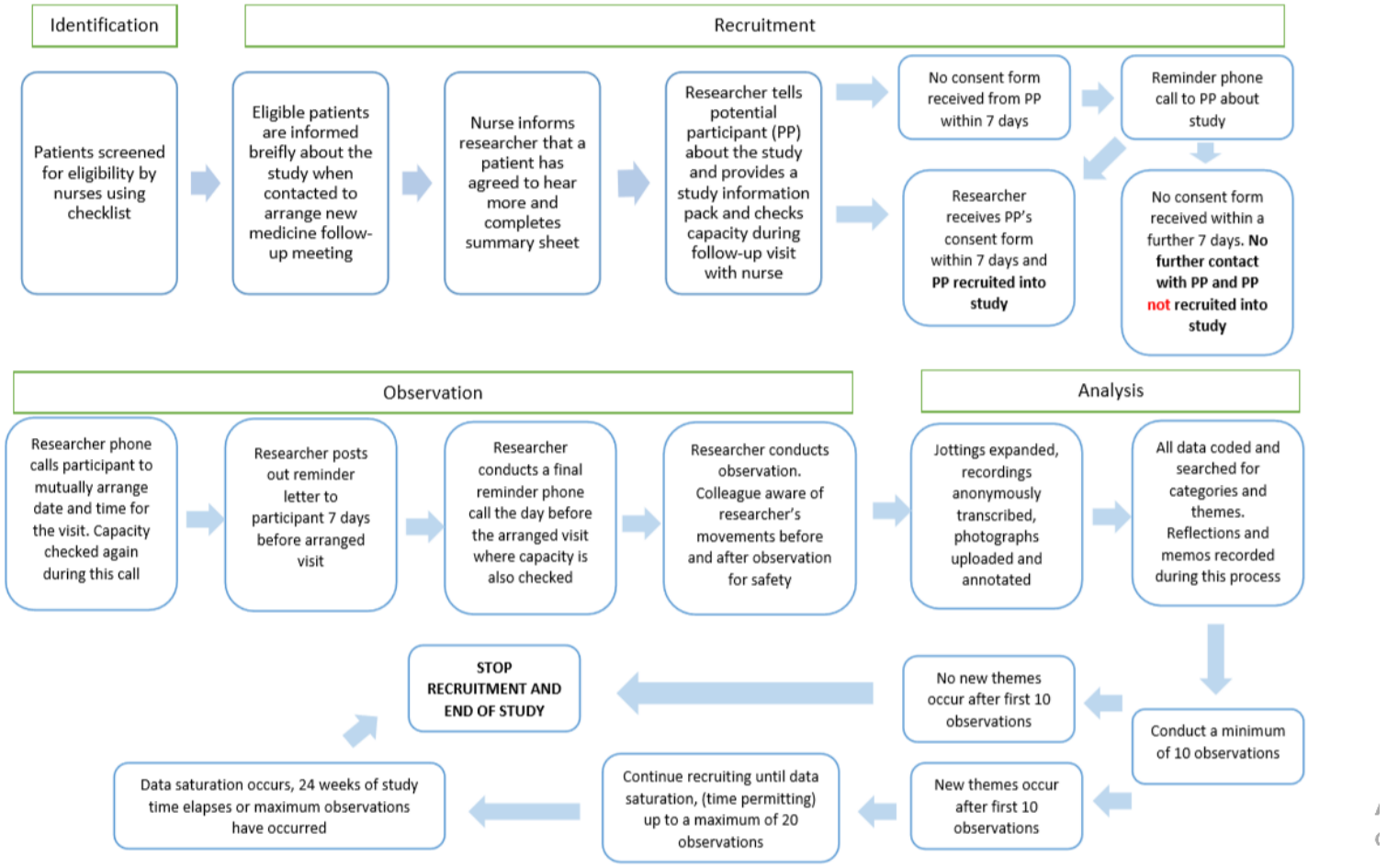
Kind Regards,

[sig]

Elly Dann-Reed
Research Pharmacist

1

Appendix 27. Study flowchart



Appendix 28: Observation guide

Observation field notes

Observation Ref:	**Date:**	**Time started:**
Independent dementia / dyad	**(delete as appropriate)**	**Time Ended:**
Anyone else present?		
Pre-reflection key words		
Observation:		
Initial observations on field and how built engagement with participants		
Medicine info:		
House space arrangements and medicine storage and organisation		

Participant routines, relationship interactions and how medicines ordered and collected
Participant routines, relationship interactions with how medicines are managed and taken
Relationship and contact with community pharmacy, doctors and other healthcare professionals
Any changes they would like in contact and relationship with healthcare professionals (doctors/nurses/pharmacists)
Other observations worthy of note:
Post reflections key words

Appendix 29.1. Recruitment tracking sheet

Recruitment tracking sheet

Tick and date when each step is completed (if PP withdraws please mark with [WD] in red next to reference name

PP* Reference	Follow-up attended		Study pack provided		Consent form received		Follow-up phone call **		Contacted to set up appointment		Reminder letter posted ^		Telephone call day ^^		Observation completed	
	Tick	Date	Tick	Date	Tick	Date	Tick	Date	Tick	Date	Tick	Date	Tick	Date	Tick	Date
IP 1																
DY 2																
IP2 [WD]																
															...	

Notes (such as reasons for withdrawing):

*Potential Participant; **tick and date when completed where this stage is required (no form received 7 days since study pack provided);^posted to arrive 7 days before observation date; ^^day before observation date

Appendix 29.2. Observation tracking sheet

Participants' data tracking sheet

Tick and date when each step is complete

PP* Reference	Observation Date	Jottings/ short accounts written into expanded accounts		Audio recording transcribed anonymously		Photographs securely saved, annotated and deleted off camera		Confidential information filed in secure, locked drawer		Transcript and expanded accounts coded and themes noted	
		Tick	Date	Tick	Date	Tick	Date	Tick	Date	Date	Date
IP 1											
DY 2											
											...
Notes:											
*Potential Participant											

Appendix 30. HRA approval

NHS
Health Research Authority

Mrs Eleanor Dann-Reed
PhD student
University of East Anglia
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ

Email: hra.approval@nhs.net

11 August 2017

Dear Mrs Dann-Reed

Letter of HRA Approval

Study title:	**A qualitative, observation study exploring how people affected with mild-moderate dementia manage their medicines and how primary care based healthcare professionals could provide better support.**
IRAS project ID:	**222968**
Protocol number:	**EDR-DW-Rev1**
REC reference:	**17/YH/0276**
Sponsor	**University of East Anglia**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Appendix 31. REC favourable opinion

NHS
Health Research Authority

Yorkshire & The Humber - Bradford Leeds Research Ethics Committee
Jarrow Business Centre
Rolling Mill Road
Jarrow
NE32 3DT

Telephone: 0207 104 8081

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

08 August 2017

Mrs Eleanor Dann-Reed
PhD student
University of East Anglia
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ

Dear Mrs Dann-Reed

Study title:	**A qualitative, observation study exploring how people affected with mild-moderate dementia manage their medicines and how primary care based healthcare professionals could provide better support.**
REC reference:	**17/YH/0276**
Protocol number:	**EDR-DW-Rev1**
IRAS project ID:	**222968**

Thank you for your letter of 8th August, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point,

A Research Ethics Committee established by the Health Research Authority

Appendix 32. NSFT approval to commence study and letter of access

Norfolk and Suffolk NHS
NHS Foundation Trust
Research and Development
The Knowledge Centre
Hellesdon Hospital
Drayton High Road
Norwich
NR6 5BE

Telephone 01603 421255
E mail: RDofficemailbox@nsft.nhs.uk

Mrs Eleanor Dann-Reed
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ

20th September 2017

Dear Mrs Dann-Reed

Re: NSFT Letter of Access for research - RD #17 222968 Living with dementia and managing medicines

This letter should be presented to each participating organisation before you commence your research at that site. The participating organisation is: **Norfolk and Suffolk NHS Foundation Trust**.

In accepting this letter, each participating organisation confirms your right of access to conduct research through their organisation for the purpose and on the terms and conditions set out below. This right of access commences on **7th September 2017** and ends on **11th March 2018** unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from **Norfolk and Suffolk NHS Foundation Trust**. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving confirmation from the individual organisation of their agreement to conduct the research.

The information supplied about your role in research at the organisation has been reviewed and you do not require an honorary research contract with the organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out. Evidence of checks should be available on request to the organisation.

You are considered to be a legal visitor to the organisations premises. You are not entitled to any form of payment or access to other benefits provided by the organisation or this organisation to employees and this letter does not give rise to any other relationship between you and the organisation, in particular that of an employee.

While undertaking research through the organisation you will remain accountable to your substantive employer but you are required to follow the reasonable instructions of the organisation or those instructions given on their behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by the organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with the organisations policies and procedures, which are available to you upon request, and the Research Governance Framework.

Appendix 33. Risk Assessment tool used

Risk Assessment Tool for Student Placements

Once completed by the student this form should be forwarded to the Placement Organiser who will formally confirm whether the Placement is Low Risk, Medium Risk or High Risk. Students should use this Risk Assessment Tool to log or 'flag' issues prior to the commencement of the placement.

Student and Placement Details			
Surname	First name		Registration Number
Name of Placement Provider			
Location			
Risk Factors	**Risk? (high, medium or low)**	**Action necessary? Control measures required.**	**Action complete?**
Assessment e.g. is the placement provider involved in assessing students in any way?			
Work Factors e.g. does it involve hazardous substances, manual handling, entering laboratories, workshops, using machinery or research equipment, working alone? e.g. will a Criminal Records Bureau check be required (where working with vulnerable groups)?			
Travel/ transportation factors e.g. levels of travel during placement, including driving and commuting; risky local transport facilities, does the placement itself involve using vehicles?			
Location and/or regional factors e.g. Foreign Office advice (in terms of risk)? Availability of services, like emergency services?			
Environmental & health factors e.g. climate; infectious diseases etc			
Individual student factors Do you feel that there are any matters which need to be given special consideration in relation to health, a disability, linguistic ability, cultural awareness?			
Insurance limitations Does the placement provider have appropriate public liability insurance? If in any doubt consult the University's Insurance Manager.			

Formal Confirmation of Level of Risk (this section to be completed by Placement Organiser/Tutor)		
Is a site safety visit required prior to approval? Yes ☐ No ☐	Are risks tolerable so placement can be authorised? Yes ☐ No ☐	
Level of Risk: High ☐ Medium ☐ Low ☐	Signed: Print Name:	Date:

1

Appendix 34. Excerpt from peer review outcome at local NSFT committee.

Norfolk and Suffolk NHS
NHS Foundation Trust
Research and Development
The Knowledge Centre
Hellesdon Hospital
Drayton High Road
Norwich
NR6 5BE

Telephone 01603 421255
E mail: RDofficemailbox@nsft.nhs.uk

Ms Elly Reed
Medicines Management Research Group
School of Pharmacy
University of East Anglia
Norwich
NR4 7TJ

3rd March 2017

Dear Elly,

Re: An exploration of how people affected with mild-moderate dementia manage their medicines and how community pharmacies could provide better support

Thank you for submitting the above project for local research peer review. The Committee reviewed the application on the meeting of the 23rd February 2017 and has made the following comments:

Background and rationale

- The committee suggested including an explanation regarding what and where community pharmacies are, what they do and what types of services that can be offered.
- The committee suggested including what gap the proposed study will fill from the literature review undertaken.
- The committee recommended including references where claims are being made in the protocol.
- The committee queried what research question is being asked by the proposed study as there are only aims and objectives stated.
- The committee recommended including a rationale for the chosen sample size.

Research design/methodology (including analysis)

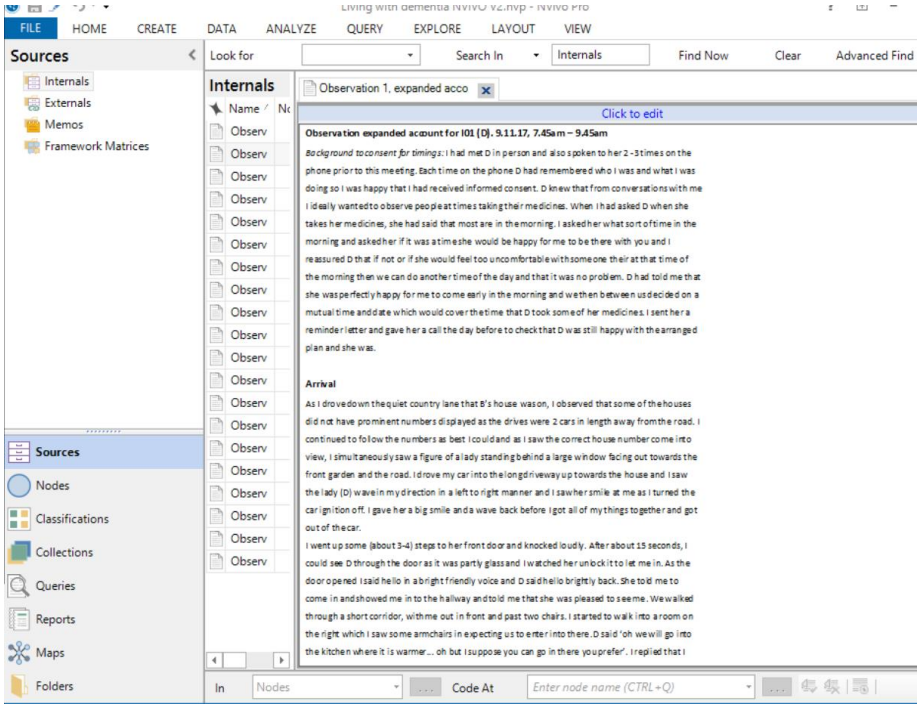
The committee felt that the presence of an unknown researcher in a vulnerable persons home for multiple hours in the evening to be intrusive and may not provide a naturalistic environment for the researcher to observe usual practice. The committee would like the researcher to justify what this approach will bring to the research compared to other data collection methods such as a carer diary about medication management.

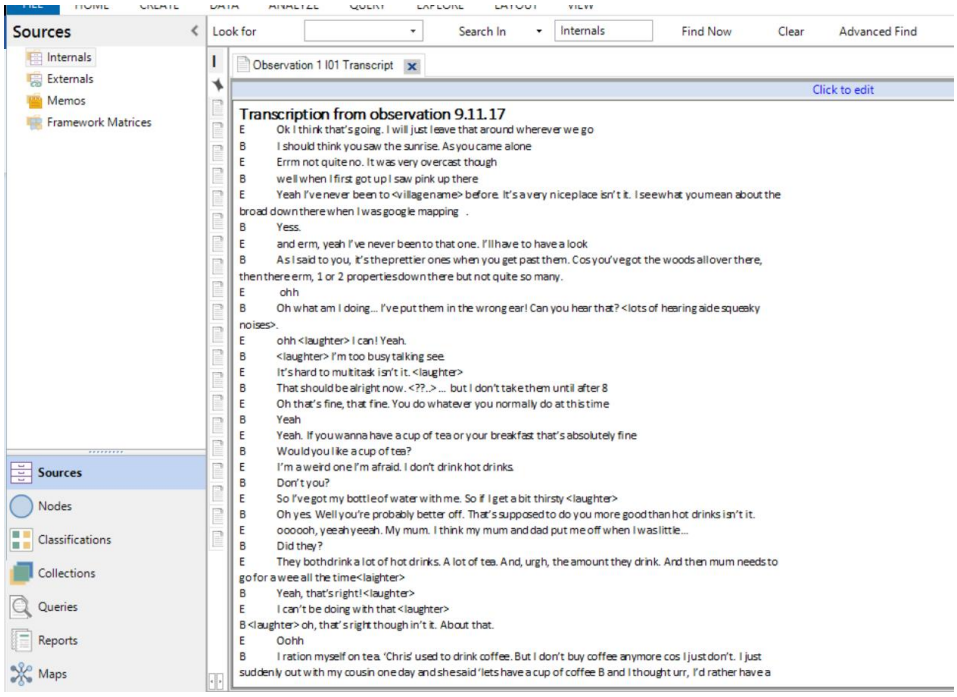
The committee suggested to break down the aims and objectives into primary and secondary aims.

Appendix 35. Example of how thematic analysis was used

Step 1: Familiarising with the data

Transcripts and expanded observation account for observation 1 were imported into the computer software NVivo 11 and read and reread to familiarise myself with the data. Transcribing the audiorecordings and writing the detailed accounts myself also helped with this.



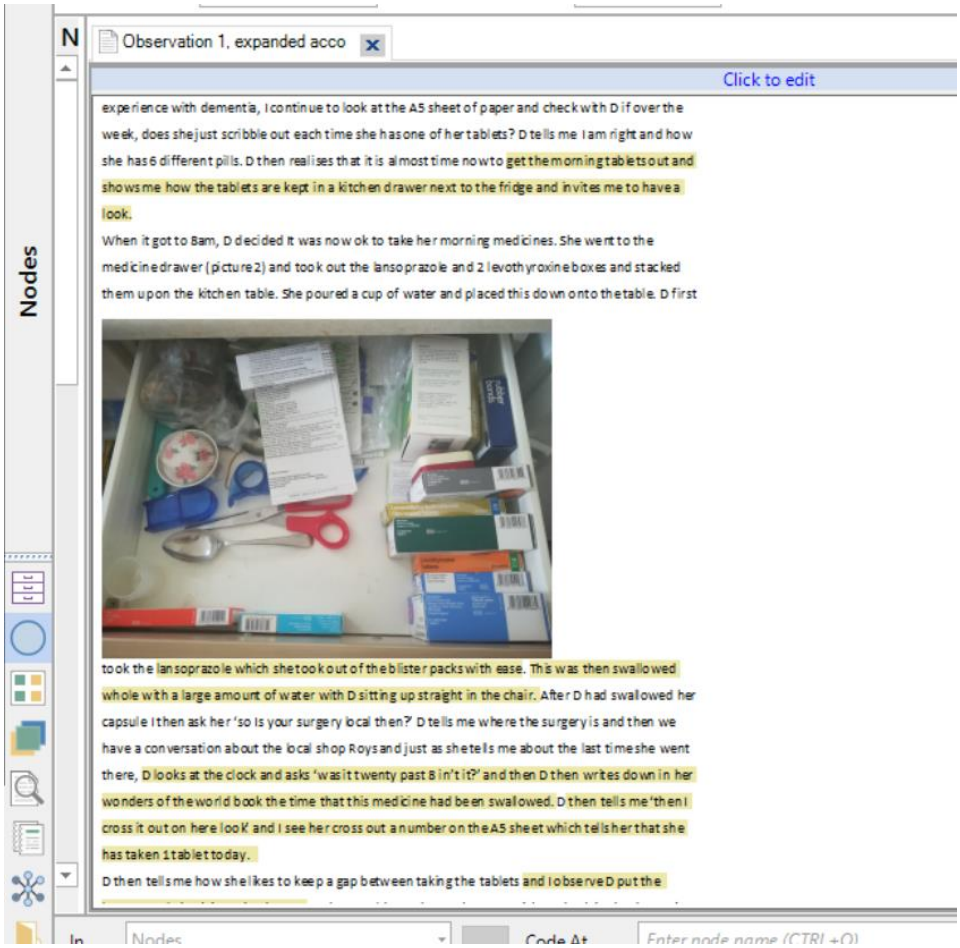


Whilst doing this, any initial thoughts, questions or vague concepts were recorded in my research diary (see Excerpt 1).

"Thinking back to this observation whilst reading the transcript, I thought IO1 was managing well with the medicines and had various people visit her so not too isolated. It was sad hearing the familial problems she has had and I hope it gets sorted as she will need increasing support as the dementia gets worse. I liked her little diary which was pocket size which meant that she could take it anywhere and show anybody. It was interesting seeing her coping mechanism for knowing when she had taken her different medicines throughout the day. Could some sort of pen/paper version be developed to be given to all patients? Could it benefit others like her? (especially as the generation with dementia are not so tech savvy so pen and paper may work better)." **(Excerpt 1)**

Step 2: Generating codes

Once I felt familiarised with the dataset from observation 1, I began coding the data using open coding. Any segment of text (or picture in the expanded accounts) which felt of relevant to the research question or added context were coded. At this early stage, codes were not labelled so that they were kept in their purest form (level 1 coding). Each yellow highlight in the picture below is a different code.



If any of the codes were very long, then I edited the code name to be shorter so the overall list of codes would be easier to manage. This observation account had 31 initial codes documented.

Whilst I was doing this level 1 coding, I was also recording in my research diary any thoughts, questions or possible immerging themes or concepts. The table below (Excerpt 2) is an excerpt from my diary which shows how I linked the expanded accounts and transcripts together for each observation in order to provide as much context as possible.

Key theme	transcription	observations
Weather, area and hearing aid	Find out that D wears a hearing aid (as puts in wrong ears).	Quiet country lanes reflect the area D lives in. Could add to isolation. Steps could be difficult for D as dementia progresses and may also deter D from leaving house.
Husband dying	D explains how she doesn't drink coffee anymore as husband used to drink it and he's now not here to share it with her as he died 17 years ago. D described in detail what happened when he died. Shows this moment in her life is still very vivid to her even though it was so long ago. D obviously still misses the husband and must have an impact on her everyday life.	The tear in her eye reinforces how much she still misses him and probably enhances the loneliness felt.
Use of It/ this for dementia	D uses 'she's got this' and 'it catches anybody' to refer to dementia. Why doesn't she use the word dementia? Embarrassed by stigma? Can't remember the word? Some other reason? **May show more normalising in PWD may be needed. And reassurance that OK to say it.**	
villagers	D describes about some of the villagers and says how 'village people aren't very nice you know'. The way she talks about them hints that she doesn't get on with some in her village and doesn't have support from them. **Could comm pharmacies have inut here to ensure support for all villagers?**	
Wonders of the world diary/book	D explains how she got this 'dear little book' with the 'peoples friend' magazine' She writes down what time she gets up and what time she goes to bed and anything important she puts in the middle. D says how she 'don't mind paying for it'. **Could we develop a diary specific for dementia and managing daily life that they can buy or be issues as part of a dementia service or intervention? Size of diary should be kept in mind. Should be small enough to easily fit in a pocket or bag so can be taken everywhere.** D describes how the diary has helped her manage her forgetfulness and gives an analogy of when she 'did a complete blank and didn't know what day it was' and used the diary to find out the date. A very handy thing to be able to look in. D gives another analogy how she has used the diary to work out that she has already taken her pills for the day and doesn't need to take anymore. **Therefore, diaries may help reduce overdoses (if used properly by patient)**	

(Excerpt 2)

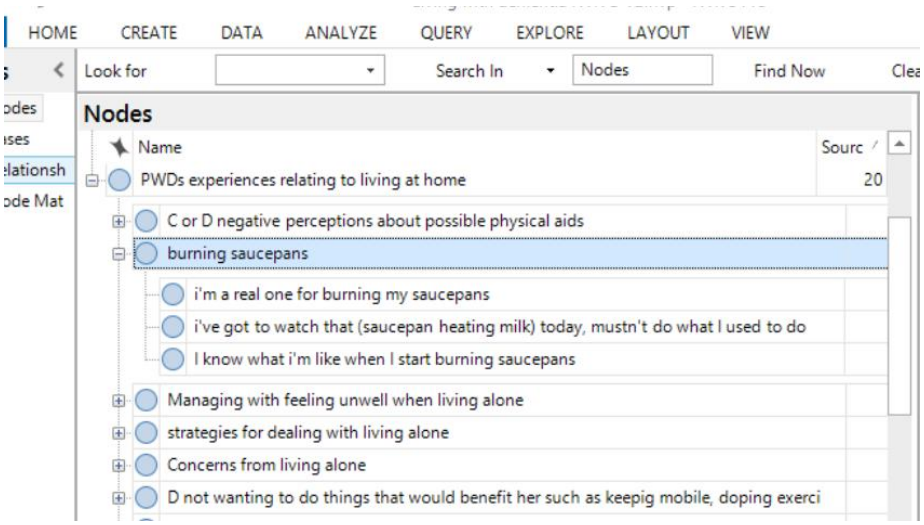
At the end of this intensive coding, documenting and thought process, I reviewed what I had written and what the key overall themes from this observation were. I recorded these at the bottom of the table in my diary for clarity and for quick reference further down the line (Excerpt 3).

	medicine taking. She rationalises how she takes then as if she takes too early, she wakes up too early in the morning which shows awareness of her tablets. D then says the times in the diary are sorta the times of waking up and going to bed. This contradicts what she said earlier and also what I have observed today with writing down the time of taking her morning tablets. Is D clear herself what the times are??	
Family	I hear about her early years in the house with young children and about her brother and how once out the blue he rang up to tell her 'I don't wanna, we don't nothing to do with you' *This happened a long time ago as was when husband was ill which was 17 years ago*	
	Stiff front door handle. Another reason D may subconsciously be put off wanting to leave the house and may get harder as time goes on. Talked more about cats and showed me her deceased cat. Really reinforced how much she loves and cares for cats and how she misses hr deceased cat. A way she copes with the lonliness?	

Themes from this observation: Strict/ regimented medicine routine
Difficulties titrating new medicine
Supportive neighbours and close family
Medicine shapes/colours/ names
Negative association with dementia and not saying the words
People to be more dementia friendly and aware
Close relationship to pets/ cats
Managing other comorbidities and cats problems
Use of diary and sheet for reminders- look at each day
Easy access of medicines and everything important to D visually there

(Excerpt 3)

Once I had completed this process, I began level 2 coding which involved placing the 164 combined initial codes from the transcript and expanded account into more manageable categories. For example, I01 mentioned about burning saucepans on 3 separate occasions and so there were grouped into the category 'burning saucepans'.



Steps 1 and 2 were then repeated for each new observation.

Step 3: Constructing themes

From observation 2 onwards, I was then able to start looking for themes which were apparent across the datasets. With the help of the tables and summary lists I was producing from each observation in step 2, I was able to easily identify the themes which were reoccurring. As these possible themes or 'candidate themes' began to emerge, I was able to begin grouping the categories into broader groups which became my first potential themes. For example, the 'burning saucepans' category was placed into the candidate theme 'PWDs experiences relating to living at home' along with a number of other categories (see map 1).

Step 4: Reviewing potential themes

As the number of observations increased and my dataset grew, more of these candidate themes emerged and became more clarified. Documenting my thoughts and findings within the research diary helped to shape the candidate themes into my final themes. These were my potential final themes:

- HOW ROUTINE IS USED IN PWD LIVING AT HOME
    - Having a specific medicine routine
    - Storing medicines or other items of importance in specific areas where their visibility aids their remembering
    - Having a day routine where the medicines are a part of this routine
    - Being organised and methodical and using reminder methods

- HOW SUPPORT IS IMPORTANT TO PWD AND HOW IS COMES IN MANY FORMS
    - Carer
    - Close family
    - Neighbours
    - Friends
    - Healthcare professionals
    - Others (gardener, hairdresser)

- PWDS EXPERIENCES RELATING TO LIVING AT HOME
    - Isolation
    - Loneliness
    - Finance
    - Cooking and eating
    - How dementia affects the person and those around them
    - Inability to do day to day tasks (shopping, read, crosswords)

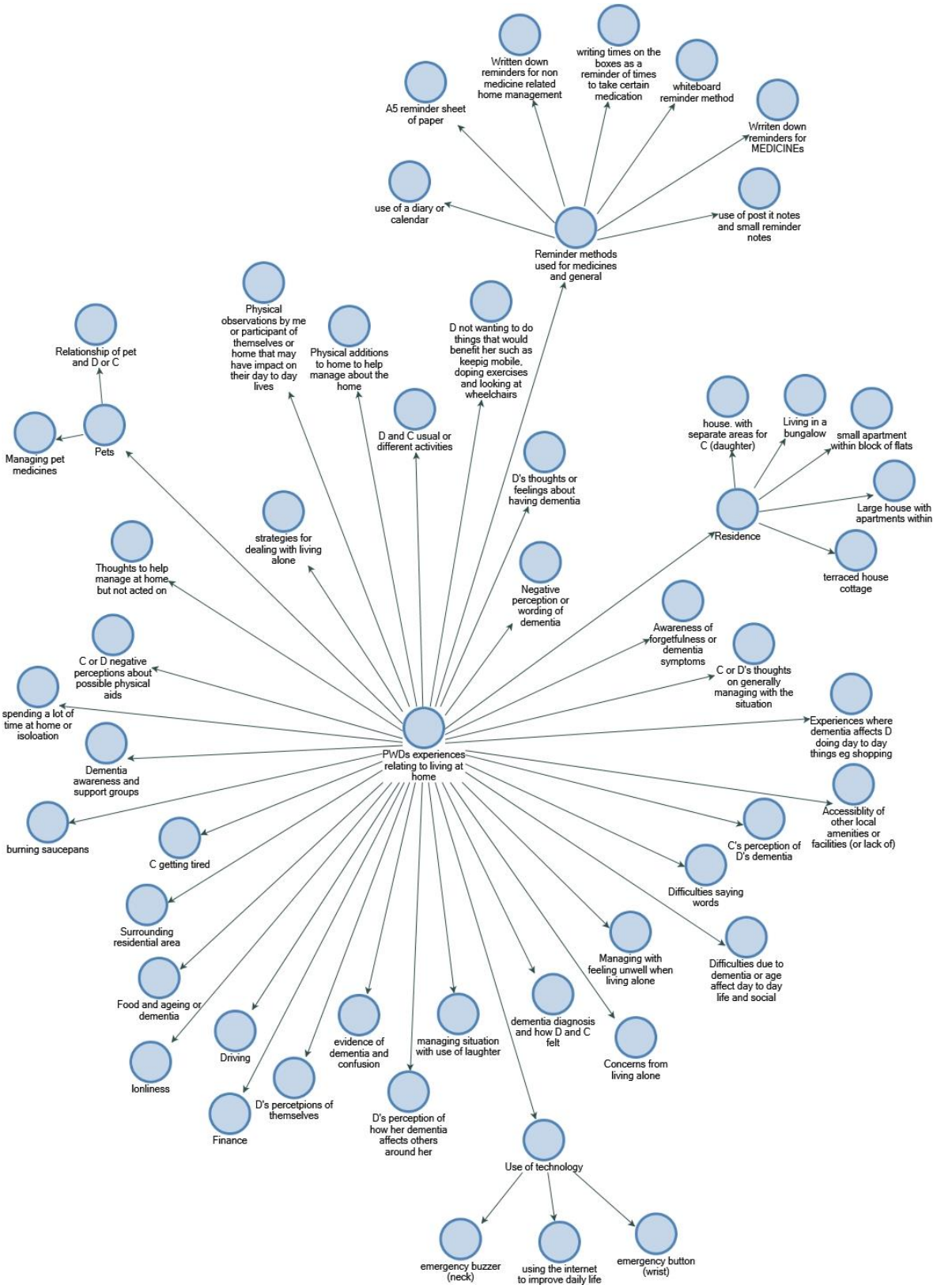
- PWD THOUGHTS AND EXPERIENCES ABOUT THEIR MEDICINES
    - Co-morbidities
    - Carer medicines and co-morbidities
    - Pet medicines
    - Remembering / pronouncing names

    - Packaging
    - Complicated regimes
    - Side effects
    - Remembering tabs and to administer tabs

- EXPERIENCES WITH HEALTHCARE
    - Pharmacy
    - GP surgery
    - (colostomy bag provider)
    - NHSFT Hospital
    - Local University hospital
    - Ambulance service

Step 5: Defining and naming themes

As I began to write my analysis down, the themes became more defined and evolved into the final themes presented in chapter 5.


Written down reminders for non medicine related home management
writing times on the boxes as a reminder of times to take certain medication
whiteboard reminder method
A5 reminder sheet of paper
Wrriten down reminders for MEDICINEs
use of a diary or calendar
use of post it notes and small reminder notes
Reminder methods used for medicines and general
Physical observations by me or participant of themselves or home that may have impact on their day to day lives
Physical additions to home to help manage about the home
D not wanting to do things that would benefit her such as keepig mobile, doping exercises and looking at wheelchairs
Relationship of pet and D or C
Pets
Managing pet medicines
D and C usual or different activities
D's thoughts or feelings about having dementia
house. with separate areas for C (daughter)
Living in a bungalow
small apartment within block of flats
Large house with apartments within
Residence
terraced house cottage
strategies for dealing with living alone
Thoughts to help manage at home, but not acted on
Negative perception or wording of dementia
Awareness of forgetfulness or dementia symptoms
C or D negative perceptions about possible physical aids
C or D's thoughts on generally managing with the situation
spending a lot of time at home or isoloation
Experiences where dementia affects D doing day to day things eg shopping
Dementia awareness and support groups
PWDs experiences relating to living at home
Accessiblity of other local amenities or facilities (or lack of)
burning saucepans
C's perception of D's dementia
C getting tired
Difficulties saying words
Surrounding residential area
Managing with feeling unwell when living alone
Difficulties due to dementia or age affect day to day life and social
Food and ageing or dementia
dementia diagnosis and how D and C felt
Driving
evidence of dementia and confusion
managing situation with use of laughter
Concerns from living alone
lonliness
D's percetpions of themselves
Finance
D's perception of how her dementia affects others around her
Use of technology
emergency buzzer (neck)
using the internet to improve daily life
emergency button (wrist)

(Map 1)